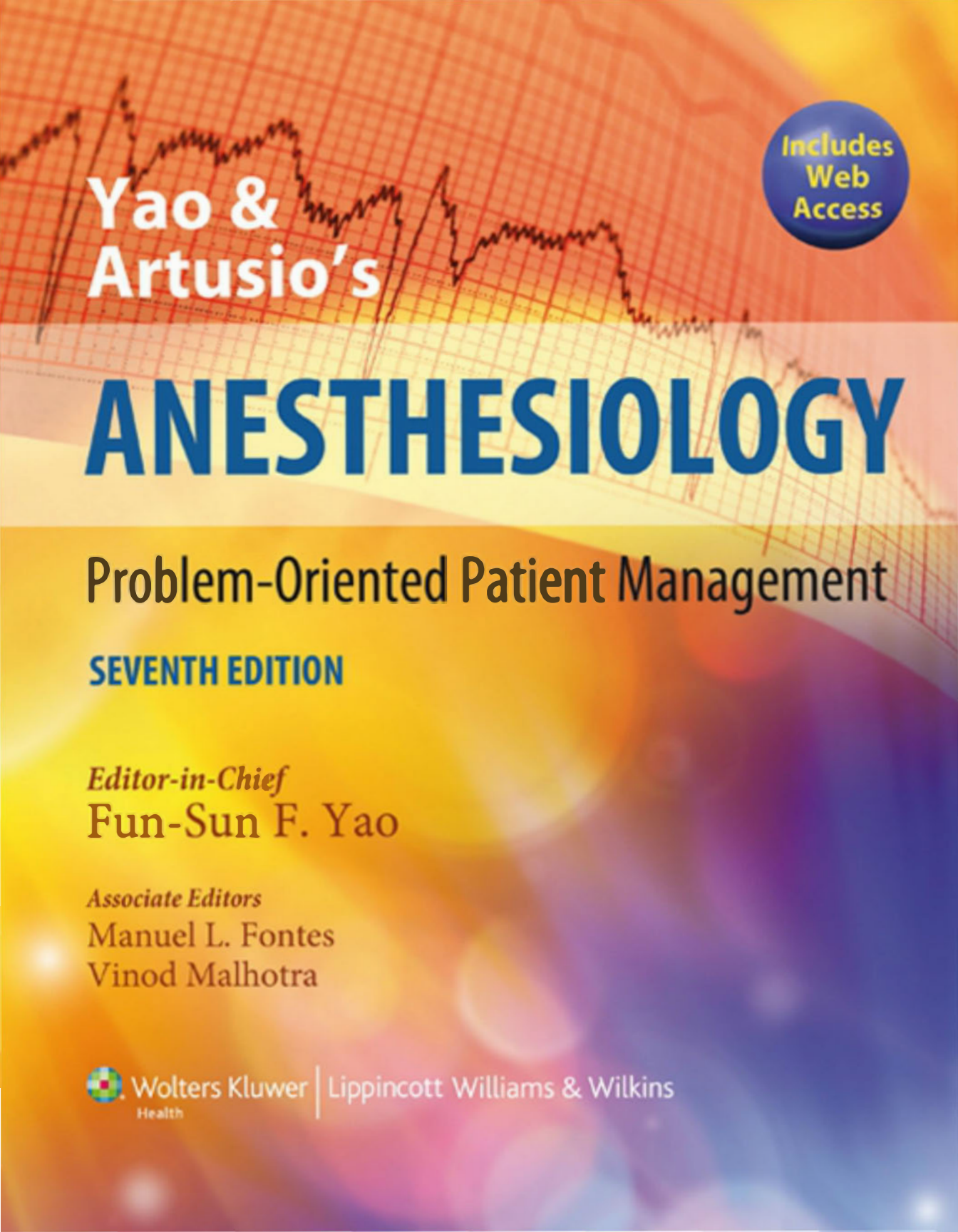
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Problem-Oriented Patient Management
SEVENTH EDITION
Editor-in-Chief
Fun-Sun F. Yao
Associate Editors
Manuel L. Fontes
Vinod Malhotra
Wolters Kluwer Health
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YAO & ARTUSIO'S

ANESTHESIOLOGY

PROBLEM-ORIENTED PATIENT MANAGEMENT

Seventh Edition

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This book is dedicated
to
Joseph F. Artusio Jr., MD
who
has taught us
not only to be good anesthesiologists
but also
to become better persons.

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PREFACE

Important advances in surgical procedures and in the clinical practice of anesthesiology have prompted the production of a new edition of this text. The book has been published in five languages: English, German, Japanese, Chinese, and Portuguese. The remarkable popularity of the first six editions in the anesthesiology community both in the United States and abroad encouraged us to update and expand its subject matter. The seventh edition is written to further improve anesthesia management for sophisticated surgery.

As with our previous editions, *Yao & Artusio's Anesthesiology: Problem-Oriented Patient Management* was written to present a group of important clinical entities covering the most critical anesthetic problems. It is intended to provide logical and scientific fundamentals for individualized patient management.

In this seventh edition, *Yao & Artusio's Anesthesiology* is organized by organ systems into 12 sections consisting of 62 chapters. Each chapter begins with a brief case presentation, followed by essential problems of each disease covering four areas: (1) pathophysiology and differential diagnosis; (2) preoperative evaluation and preparation; (3) intraoperative management; and (4) postoperative anesthetic management. Using a question-and-answer format, the book is designed to stress anesthetic problems and to give the anesthesiologist the opportunity to organize his or her own ideas of patient care. A reasonable answer, with updated references, follows each question.

To maintain the fresh quality of the textbook, approximately one-third of the seventh edition consists of new chapters or contributions by new authors. All pediatric chapters from different organ systems are regrouped to the new section of Pediatric Anesthesia to reflect the importance of this unique subspecialty. The text originally reflected the clinical experience of the Department of Anesthesiology at Weill Cornell Medical College–The New York Presbyterian Hospital. In this edition, experts from other prestigious institutions have contributed their invaluable opinions to make this book more universally acceptable and applicable. The material in the book is prepared for the education of the resident and the practicing anesthesiologist; it also serves as a review source for continuing education and for preparing for board examinations and recertification. The question-and-answer format, combined with current references, enhances its educational value.

We welcome comments, criticisms, and suggestions for future editions.

ACKNOWLEDGMENTS

I wish to express my personal gratitude to the individual contributors. This book would not have been possible without their hard work and dedication. I am grateful to the associate editors: Vinod Malhotra, MD, and Manuel Fontes, MD, for their invaluable assistance. I would like to thank our editors at Lippincott Williams & Wilkins (Wolters Kluwer), Brian Brown, Lisa McAllister, Nicole Dernoski, and Matt Gardner for their commitment to excellence. In addition, I am especially indebted to John J. Savarese, MD, for his constructive advice and support. Above all, my deepest appreciation goes to my family, Tong-Yi, Ning-Yen, Jean-Kuan, and especially to my dear compassionate wife, Baw-Chyr Peggy Yao. Her understanding, patience, and encouragement made this book possible.

Fun-Sun F. Yao, MD

SECTION I

The Respiratory System

CHAPTER 1

Asthma and Chronic Obstructive Pulmonary Disease

FUN-SUN F. YAO

A 55-YEAR-OLD MAN

with cholelithiasis was scheduled for cholecystectomy. He had a long history of asthma and developed dyspnea with only moderate exertion. He slept on two pillows. There was no peripheral edema. Arterial blood gases (ABGs) showed the following: pH 7.36; P_{CO_2}, 60 mm Hg; P_{O_2}, 70 mm Hg; CO_2 content, 36 mEq per L.

A. Medical Disease and Differential Diagnosis

1. What differential diagnosis is compatible with these symptoms?
2. What is the prevalence of asthma?
3. What is the etiology of asthma?
4. Discuss the pathogenesis of asthma.
5. What are the predisposing factors of asthmatic attacks?
6. What is the universal finding in ABGs during asthmatic attacks: Hypoxemia or CO_2 retention?
7. What changes are seen in spirometry, lung volumes, and lung capacities during an asthmatic attack?

B. Preoperative Evaluation and Preparation

1. How would you evaluate the patient preoperatively? What preoperative workup would you order?
2. How would you distinguish obstructive lung disease from restrictive lung disease by spirometry?
3. Define normal lung volumes and lung capacities and their normal values in the average adult man.
4. What are flow–volume loops? Draw flow–volume loops in a healthy subject, in a patient with chronic obstructive pulmonary disease (COPD), and in a patient with restrictive lung disease.
5. Define closing capacity (CC) and closing volume (CV). What is the normal value of CV?
6. What are the effects of age and posture on functional residual capacity (FRC) and CC?
7. What are the effects of anesthesia on FRC and CC?
8. Why is the FRC important in oxygenation?
9. Are there methods to measure FRC and CV?
10. Give the equations for shunt ($\dot{Q}s/\dot{Q}T$) and dead space/tidal volume (VD/VT). What are their normal values?
11. Interpret the following ABGs: pH, 7.36; PCO_2, 60 mm Hg; PO_2, 70 mm Hg; CO_2 content, 36 mEq per L.
12. What are the common physiologic causes of hypoxemia?
13. Would you order any special preoperative preparations for asthmatic patients with COPD?
14. How long would you postpone elective surgery if the patient had a recent upper respiratory infection (URI)?
15. What medicines would you expect the patient to have taken in the past or be taking at the present time?
16. Would you order preoperative steroid preparation? Why?
17. What is the onset of action of intravenous steroid therapy in asthma?
18. What are the effects of H_2-receptor antagonists on patients with asthma?
19. How would you premedicate the patient? Why?

C. Intraoperative Management

1. What are the disadvantages of administering atropine to the patient with asthma?
2. If the patient had a severe asthmatic attack in the operating room before the induction of anesthesia, would you proceed with the anesthetic or postpone the surgery?
3. The patient did not have an asthmatic attack in the operating room. How would you induce anesthesia? Would you use a laryngeal mask airway (LMA) instead of an endotracheal tube?
4. Why would you use propofol for induction of anesthesia?
5. Would you use thiopental, methohexital, etomidate, or ketamine for induction?
6. Would you use lidocaine for intubation?
7. If this is an emergency surgery and rapid sequence induction is indicated, how would you induce anesthesia in this patient?
8. What is your choice of agents for maintenance of anesthesia? Why?
9. What are the mechanisms of volatile anesthetics that produce bronchodilation?

10. Why would you choose an inhalational instead of an intravenous technique?
11. Is regional anesthesia better than general anesthesia in this situation?
12. Which muscle relaxants would you use? Why?
13. In the middle of surgery, the patient developed a severe wheezing attack. How do you manage it?
14. How would you give β_2-agonists? What is their mechanism of action on asthma?
15. Would you administer aminophylline? How does aminophylline relieve bronchospasm? What is the mechanism of action? What are the toxic effects of aminophylline?
16. If the patient does not respond to the aforementioned treatment and becomes cyanotic, what would you do?
17. What are the differential diagnoses of intraoperative bronchospasm?
18. The asthmatic attack was finally relieved, and the surgery was completed. The patient was found to be hypoventilating. What are the common causes of hypoventilation? Would you like to reverse the muscle relaxant?

D. Postoperative Management

1. Would you extubate the patient with asthma while he or she was deeply anesthetized?
2. When the patient cannot be extubated early in the recovery room, how would you keep the endotracheal tube in place without causing bronchoconstriction?
3. In patients with asthma, are opioids contraindicated for postoperative pain control?
4. The patient was breathing well and was extubated. How much oxygen would you give to this patient who has asthma and COPD in the recovery room?

A. Medical Disease and Differential Diagnosis

A.1. What differential diagnosis is compatible with these symptoms?

The differential diagnoses of wheezing and dyspnea include bronchial asthma; acute left ventricular failure (cardiac asthma); upper airway obstruction by tumor or laryngeal edema; and endobronchial disease such as foreign body aspiration, neoplasms, bronchial stenosis, carcinoid tumors, recurrent pulmonary emboli, chronic bronchitis, eosinophilic pneumonias, chemical pneumonias, and occasionally polyarteritis. To differentiate asthma from other diseases with wheezing and dyspnea is usually not difficult. The triad of dyspnea, coughing, and wheezing, in addition to a history of periodic attacks, is quite characteristic. A personal or family history of allergic disease is valuable contributory evidence. A patient with long-standing asthma may develop chronic obstructive lung disease and suffer from exertional dyspnea and orthopnea. Cardiac asthma is a misnomer and refers to acute left ventricular failure. Although the primary lesion is cardiac, the disease manifests itself in the lungs. The symptoms and signs may mimic bronchial asthma, but the findings of moist basilar rales, gallop rhythms, blood-tinged sputum, peripheral edema, and a history of heart disease allow the appropriate diagnosis to be reached.

Fauci AS, Braunwald E, Kasper DL, et al., eds. *Harrison's Principles of Internal Medicine*, 17th ed. New York: McGraw-Hill; 2008:1596–1607.

Gould BE. *Pathophysiology for the Health Professions*. 3rd ed. Philadelphia: Saunders; 2006: 393–398.

A.2. What is the prevalence of asthma?

Asthma is one of the most common chronic diseases globally and currently affects approximately 300 million people. The prevalence of asthma has risen in affluent countries over the last 30 years but now appears to have stabilized, with around 10% to 12% of adults and 15% of children affected by asthma. The prevalence in the United States is 6.7% of the population. It occurs at all ages, with a peak age of 3 years. Approximately half of patients develop asthma before age 10 and another third before age 40. In childhood, there is a 2:1 male/female preponderance, which equalizes by age 30.

Fauci AS, Braunwald E, Kasper DL, et al., eds. *Harrison's Principles of Internal Medicine*. 17th ed. Philadelphia: McGraw-Hill; 2008:1596–1607.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone; 2008:163–167.

The state of asthma in America: two landmark Surveys. 2009. Available from http://www.asthmainamerica.com/.

A.3. What is the etiology of asthma?

Asthma is a heterogeneous disease with interplay between genetic and environmental factors; its etiology is difficult to define. The common denominator that underlies the asthmatic diathesis is a nonspecific hyperirritability of the tracheobronchial tree. Clinically, asthma is classified into two groups: allergic (extrinsic) and idiosyncratic (intrinsic). Allergic asthma is usually associated with a personal or family history of allergic diseases, positive skin reactions to extracts of airborne antigens, and increased levels of immunoglobulin E (IgE) in the serum. Immunologic mechanisms appear to be causally related to 25% to 35% of all cases and contributory in another 33%. Idiosyncratic asthma cannot be classified on the basis of immunologic mechanisms, and it is probably due to abnormality of the parasympathetic nervous system. Bronchospasm is provoked when certain agents stimulate tracheobronchial receptors. Intraoperative bronchospasm is probably usually cholinergically mediated. Afferent receptors in the bronchial mucosa can be an initiating event, although such an event is not always identifiable. Efferent parasympathetic fibers travel to bronchial smooth muscle and can then result in bronchoconstriction by stimulation of the M3 cholinergic receptors on bronchial smooth muscle. After release of acetylcholine (Ach) at the M3 receptor, the Ach will stimulate the M2 muscarinic receptor, which is an inhibitory receptor that limits further release of Ach. Alterations of M2 receptor function may contribute to bronchospasm.

Fanta CH. Asthma. *N Engl J Med*. 2009;360:1002–1014.

Fauci AS, Braunwald E, Kasper DL, et al., eds. *Harrison's Principles of Internal Medicine*. 17th ed. New York: McGraw-Hill; 2008:1596–1607.

A.4. Discuss the pathogenesis of asthma.

Asthma is a chronic disease characterized by chronic airway inflammation, reversible expiratory airflow obstruction resulting from narrowing of the airways in response to various stimuli, and airway hyperreactivity. The common denominator underlying the asthmatic diathesis is a nonspecific hyperirritability of the tracheobronchial tree. The basic mechanism of persistent subacute airway hyperirritability remains unknown. The most popular hypothesis is subacute airway inflammation. Even when asthmatics are in remission, bronchial biopsy reveals infiltration by inflammatory cells and epithelial shedding from the mucosa. After exposure to an initiating stimulus, inflammatory cells (mast cells, eosinophils, T-lymphocytes, macrophages, basophils, neutrophils, and platelets) and structural cells (epithelial cells, fibroblasts, and airway smooth muscle cells)

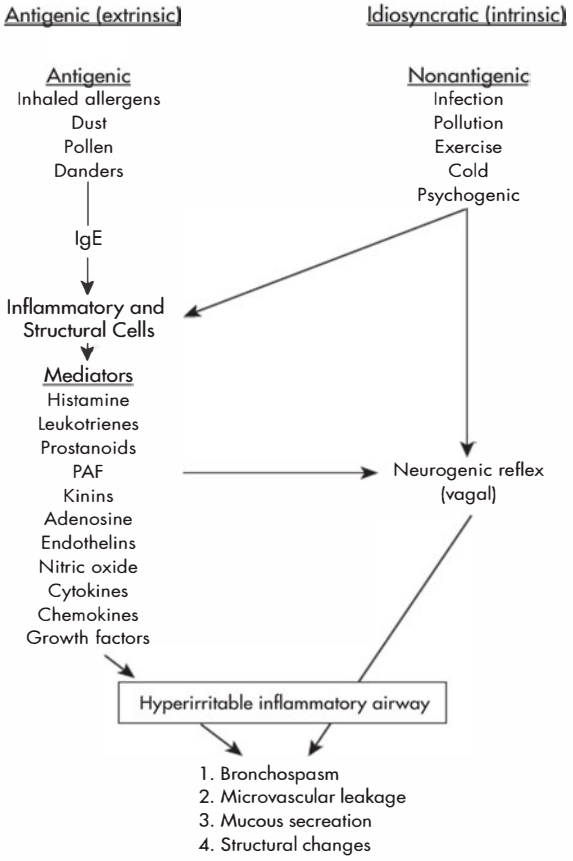

Figure 1.1 The pathogenesis of bronchial asthma. IgE, immunoglobulin E.

can be activated to release various mediators that lead to contraction of airway smooth muscle (bronchospasm), vascular congestion, increased capillary permeability (edema of bronchial mucosa), and thick tenacious secretions, thereby evoking an intense inflammatory reaction (Fig. 1.1). The net result is a reduction in airway diameter, an increase in airway resistance, decreased forced expiratory volumes and flow rates, hyperinflation of the lungs and thorax, increased work of breathing, alterations in respiratory tract muscle function, mismatched ventilation/perfusion, and altered blood gases.

Fanta CH. Asthma. *N Engl J Med.* 2009;360:1002–1014.

Fauci AS, Braunwald E, Kasper DL, et al., eds. *Harrison's Principles of Internal Medicine.* 17th ed. New York: McGraw-Hill; 2008:1596–1607.

A.5. What are the predisposing factors of asthmatic attacks?

- *Allergens*. Inhaled allergens are common triggers of asthma. Airborne allergens are able to activate mast cells with bound IgE, directly leading to the immediate release of a bronchoconstrictor.

- *Infections*. Respiratory tract infections are among the most common stimuli that evoke acute asthmatic attacks.
- *Pharmacologic stimuli*. The drugs most commonly associated with the induction of acute asthmatic attacks are aspirin, coloring agents such as tartrazine, β-adrenergic antagonists, and sulfiting agents. Aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs), such as indomethacin, mefenamic acid, ibuprofen, fenoprofen, flufenamic acid, naproxen, and phenylbutazone, make the asthma worse because of inhibition of prostaglandin G/H synthetase 1 (cyclooxygenase type 1). β-Adrenergic blockers commonly worsen asthma, and their use may be fatal. All nonspecific β-blockers should be avoided. Nevertheless, the ultra–short-acting β-1 selective antagonists landiolol and esmolol can be safely used perioperatively in patients with airway hyperreactivity.
- *Environment and air pollution*. Some types of asthma, such as Tokyo-Yokohama or New Orleans asthma, tend to occur in individuals who live in heavy industrial or dense urban areas.
- *Occupational factors*. Various compounds used in industry can cause asthma in susceptible individuals. Various names have been applied to this condition, such as meat wrapper's asthma, baker's asthma, and woodworker's asthma.
- *Exercise*. Asthma can be induced or made worse by physical exertion. The mechanism is linked to hyperventilation, which results in increased osmolality in airway lining fluid and triggers mast cell mediator release, resulting in bronchoconstriction.
- *Emotional stress*. Asthma can be induced by bronchoconstriction through the cholinergic reflex pathway.

Fauci AS, Braunwald E, Kasper DL, et al., eds. *Harrison's Principles of Internal Medicine*. 17th ed. New York: McGraw-Hill; 2008:1596–1607.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone; 2008:163–167.

Yamakage M, Iwasaki S, Jeong SW, et al. Beta-1 selective adrenergic antagonist landiolol and esmolol can be safely used in patients with airway hyperreactivity. *Heart Lung*. 2009;38:48–55.

A.6. What is the universal finding in ABGs during asthmatic attacks: Hypoxemia or CO_2 retention?

Hypoxemia is a universal finding during asthmatic attacks. However, frank ventilatory failure with CO_2 retention is relatively uncommon because CO_2 has a diffusion capacity that is 20 times higher than that of oxygen. During acute asthmatic attacks, most patients try to overcome airway obstruction and hypoxia by hyperventilation. This results in hypocarbia and respiratory alkalosis. CO_2 retention is a late finding and indicates severe and prolonged airway obstruction, as in status asthmaticus.

Fauci AS, Braunwald E, Kasper DL, et al., eds. *Harrison's Principles of Internal Medicine*. 17th ed. New York: McGraw-Hill; 2008:1596–1607.

A.7. What changes are seen in spirometry, lung volumes, and lung capacities during an asthmatic attack?

The forced vital capacity (FVC) is usually normal but may be decreased during a severe attack. The forced expiratory volume at 1 second (FEV_1) is sharply reduced, usually to less than 50% of the FVC, typically less than 40% of that predicted. The maximum midexpiratory flow rate (MMEFR) and maximum breathing capacity

(MBC) are sharply reduced as well. Residual volume (RV) is markedly increased, frequently approaching 400% of normal, and expiratory reserve volume (ERV) is moderately decreased. Therefore, FRC and total lung capacity (TLC) are increased. FRC frequently doubles.

Fauci AS, Braunwald E, Kasper DL, et al., eds. *Harrison's Principles of Internal Medicine*. 17th ed. New York: McGraw-Hill; 2008:1596–1607.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth.* 2009;103(suppl l):i57–i65.

B. Preoperative Evaluation and Preparation

B.1. How would you evaluate the patient preoperatively? What preoperative workup would you order?

The goal of preoperative evaluation is to formulate an anesthesia plan that prevents or blunts obstruction to expiratory airflow. Preoperative evaluation requires an assessment of disease severity, effectiveness of current pharmacologic therapy, and potential need for additional treatment before surgery. Key clues to severe disease include a history of frequent exacerbation, hospital visits, use of a systemic steroid, and most importantly, prior tracheal intubation and mechanical ventilation to deal with a severe attack. In addition to routine tests such as complete blood cell count, serum electrolytes, urinalysis, electrocardiogram, and coagulation screening, special attention should be paid to cardiopulmonary function: chest radiograph; pulmonary function test results, including response to bronchodilator; and baseline ABGs. A history of allergy and symptoms and signs of cardiac or respiratory failure must be checked carefully.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone; 2008:163–167.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth.* 2009;103(suppl l):i57–i65.

B.2. How would you distinguish obstructive lung disease from restrictive lung disease by spirometry?

Table 1.1 summarizes the distinctions between the two types of lung diseases. In restrictive lung disease (e.g., pulmonary fibrosis and ankylosing spondylitis), the FVC is low because of limited expansion of the lungs or chest wall, although the FEV_1 is often not reduced proportionately, because airway resistance is normal. Therefore, the FEV_1/FVC percentage is normal or high.

In obstructive lung disease (e.g., emphysema), the FEV_1/FVC is grossly reduced because the airway resistance is high. MBC and MMEFR are reduced early in small airway obstruction. MMEFR is also referred to as $FEF_{25\%–75\%}$ (forced expiratory flow). MMEFR is obtained by dividing the volume between 75% and 25% of the vital capacity (VC) by the corresponding elapsed time. Unlike FEV_1, MMEFR is independent of patient effort.

Normally, FEV_1 is more than 80% of FVC and VC should be more than 80% of predicted value. The predicted values depend on body size, age, and sex. The TLC is increased in obstructive lung disease and decreased in restrictive lung disease.

Table 1.1 Differences between Obstructive and Restrictive Lung Diseases

	OBSTRUCTIVE	RESTRICTIVE
Vital capacity	N or ↓	↓
Total lung capacity	N or ↑	↓
Residual volume	↑	↓
FEV_1/FVC	↓	N or ↑
Maximum midexpiratory flow rate	↓	N
Maximum breathing capacity	↓	N

↓, decreased; ↑, increased; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; N, normal.

However, TLC cannot be obtained by routine screening spirometry. Normal MBC is more than 125 L per minute and normal MMEFR is more than 300 L per minute.

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:250.

Crapo RO. Pulmonary function testing. *N Engl J Med*. 1994;331:25–30.

Fauci AS, Braunwald E, Kasper DL, et al., eds. *Harrison's Principles of Internal Medicine*. 17th ed. New York: McGraw-Hill; 2008:1588.

B.3. Define normal lung volumes and lung capacities and their normal values in the average adult man.

There are four basic "volumes" and four derived "capacities" that are combinations of these volumes (Fig. 1.2).

Tidal volume (VT) is the volume of air inhaled or exhaled during normal breathing. Normal VT is 500 mL or approximately 6 to 8 mL per kg.

Inspiratory reserve volume (IRV) is the maximum volume of gas that can be inhaled after a normal inspiration while at rest. Normal IRV is 2,000 to 3,000 mL.

Expiratory reserve volume (ERV) is the maximum volume of gas that can be exhaled after a normal expiration. Normal ERV is 1,000 mL.

Residual volume (RV) is the volume of gas remaining in the lungs after a forced exhalation. Normal RV is 1,500 mL.

Vital capacity (VC) is the maximum amount of gas that can be exhaled after a maximum inhalation. VC is the sum of VT, ERV, and IRV. Normal VC is approximately 60 to 70 mL per kg.

Inspiratory capacity (IC) is the maximum amount of gas that can be inhaled from the resting expiratory position after a normal exhalation. It is the sum of VT and IRV. Normal IC is 3,500 mL.

Functional residual capacity (FRC) is the remaining lung volume at the end of a normal quiet expiration. It is the sum of RV and ERV. Normal FRC is 2,500 mL or 30 to 40 mL per kg.

Total lung capacity (TLC) is the lung volume at the end of a maximum inspiration. It is the sum of VC and RV. Normal TLC is 5,000 to 6,000 mL for an adult man and 4,000 to 5,000 mL for an adult woman.

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:247.

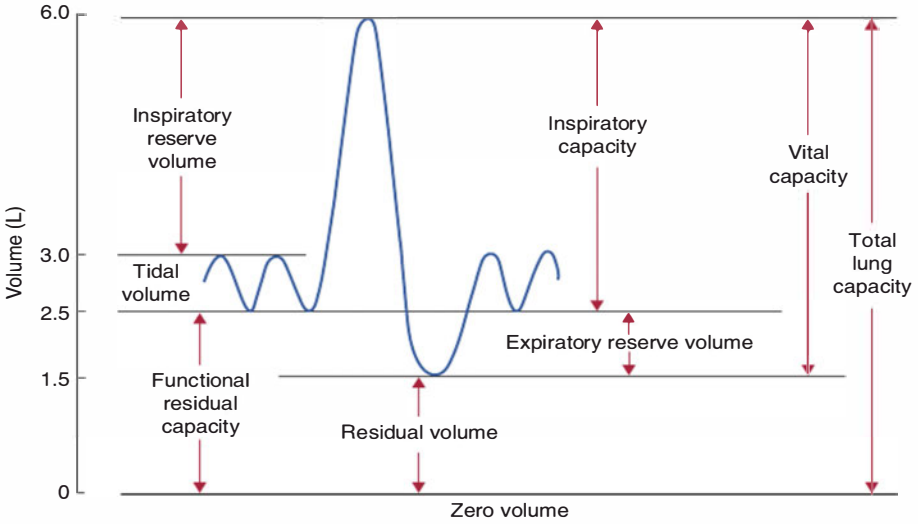

Figure 1.2 Lung volumes and lung capacities.

Fauci AS, Braunwald E, Kasper DL, et al., eds. *Harrison's Principles of Internal Medicine*. 17th ed. New York: McGraw-Hill; 2008:1586.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 6th ed. Philadelphia: Butterworth-Heinemann; 2005:33–35.

B.4. What are flow–volume loops? Draw flow–volume loops in a healthy subject, in a patient with chronic obstructive pulmonary disease (COPD), and in a patient with restrictive lung disease.

Flow–volume loops provide a graphic analysis of flow at various lung volumes. Both flow and volume are plotted simultaneously on an X–Y recorder as subjects inspire fully to TLC and then perform an FVC maneuver. This is immediately followed by maximum inhalation as fast as possible back to TLC (Fig. 1.3). The entire inspiratory portion of the loop and the expiratory curve near TLC are highly effort dependent, and the expiratory flow at 75% to 25% of VC is effort independent. The normal expiratory flow/inspiratory flow ratio at 50% of VC (mid-VC flow ratio) is approximately 1.0. This ratio is particularly useful in identifying the presence of upper airway obstruction. In patients with restrictive lung diseases such as pulmonary fibrosis and scoliosis, a reduction is seen in FVC, with a relatively normal FEV_1. The TLC is markedly reduced, and the $FEF_{25\%–75\%}$ and mid-VC flow ratio are usually normal (Fig. 1.4). In patients with obstructive lung disease, peak expiratory flow rate, $FEF_{25\%–75\%}$, and mid-VC flow ratio are reduced, but TLC is increased secondary to the increase in RV, as shown in Figure 1.4.

A variable obstruction is defined as a lesion with influence that varies with the phase of respiration. In variable extrathoracic obstructions such as vocal cord paralysis or tracheal stenosis, during forced inspiration, the respiratory flow is reduced because the negative transmural pressure inside the airway tends to collapse the airway. During expiration, the expiratory flow is reduced far less and may be normal because the positive pressure inside the airway tends to

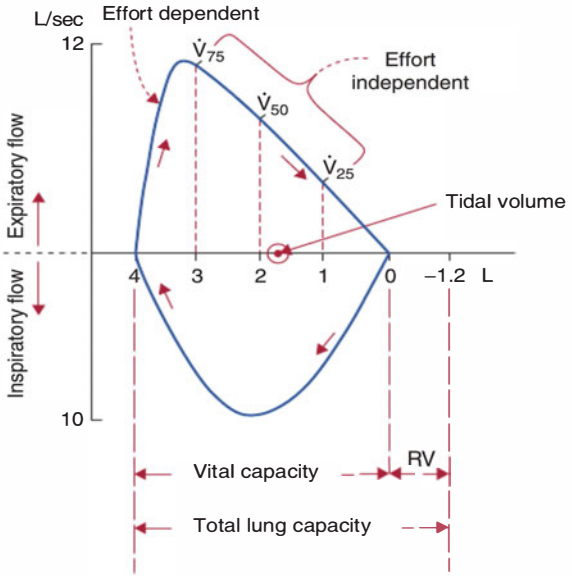

Figure 1.3 Flow–volume loop in a healthy subject. $\dot{V}_{75}$, $\dot{V}_{50}$, and $\dot{V}_{25}$ represent flow at 75%, 50%, and 25% of vital capacity, respectively. RV, residual volume. (From Goudsouzian N, Karamanian A. Physiology for the Anesthesiologist. 2nd ed. Norwalk, CT: Appleton-Century-Crofts; 1984, with permission.)

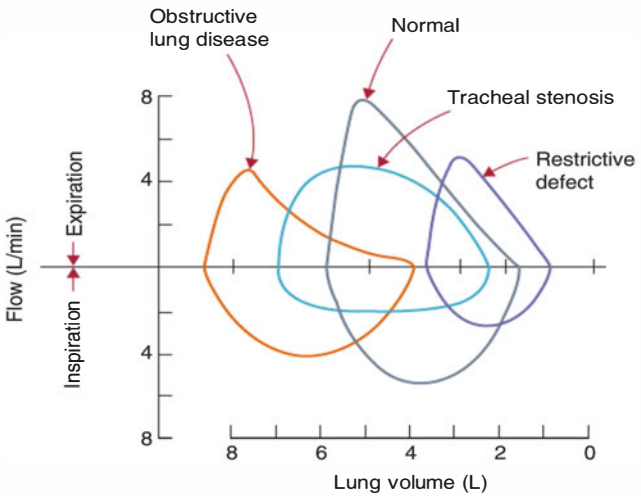

Figure 1.4 Flow–volume loops relative to lung volumes in a healthy person, a patient with chronic obstructive pulmonary disease (COPD), a patient with fixed obstruction (tracheal stenosis), and a patient with pulmonary fibrosis (restrictive defect). Note the concave expiratory form in the patient with COPD and the flat inspiratory curve in the patient with a fixed obstruction. (From Goudsouzian N, Karamanian A. Physiology for the Anesthesiologist. 2nd ed. Norwalk, CT: Appleton-Century-Crofts; 1984, with permission.)

decrease the obstruction (Fig. 1.4). On the contrary, in variable intrathoracic obstruction, the expiratory flow is markedly reduced because the high positive intrapleural pressures during forced expiration decrease airway diameter, and the inspiratory flow is far less reduced because the negative intrapleural pressure tends to increase the diameter of the airway. (Also see Fig. 21.2 in Chapter 21 Thyrotoxicosis.)

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:249, 1035.

Fauci AS, Braunwald E, Kasper DL, et al., eds. *Harrison's Principles of Internal Medicine*. 17th ed. New York: McGraw-Hill; 2008:1588.

B.5. Define closing capacity (CC) and closing volume (CV). What is the normal value of CV?

CC is the lung volume at which the small airways in the dependent parts of the lung begin to close. CC is the sum of CV and RV. CV is the volume above RV at which small airways begin to close during expiration. CV is the gas volume expelled during phase IV of the single-breath nitrogen test; it denotes the lung volume from the beginning of airway closure to the end of maximum expiration. Therefore, CV = CC – RV (Fig. 1.5).

In healthy young people, CV is approximately 10% of the VC, or 400 to 500 mL. CV and CC increase with age. CV is increased in patients with small airway disease and in chronic smokers.

Buist AS. The single-breath nitrogen test. *N Engl J Med*. 1975;293:438.

Closing volume [Editorial]. *Lancet*. 1972;2:908.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 6th ed. Philadelphia: Butterworth-Heinemann; 2005:44.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:368.

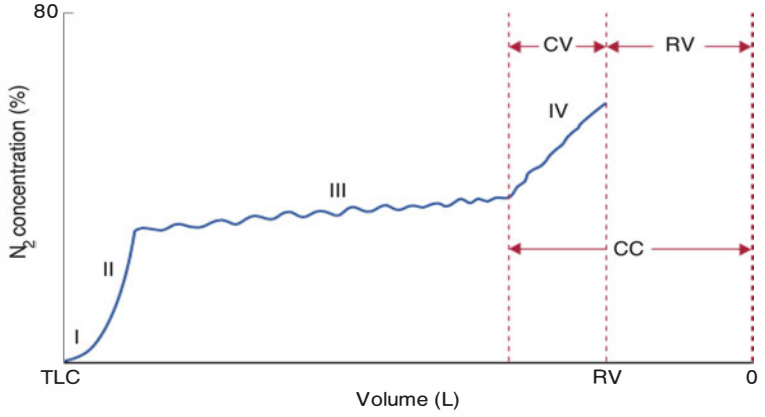

Figure 1.5 Closing volume measurement by single-breath nitrogen test. CC, closing capacity; CV, closing volume; RV, residual volume; TLC, total lung capacity.

B.6. What are the effects of age and posture on functional residual capacity (FRC) and CC?

FRC is either independent of age in adults or increases very slightly with age, increasing approximately 16 mL per year. CC, however, increases with age. Normally, CC becomes equal to FRC at the age of 66 in the upright position and at the age of 44 in the supine position.

FRC increases by approximately 30% in changing from the supine position to the upright position. CC, on the other hand, is independent of body position. It is important to remember that the effects of age on CC and posture on FRC determine whether airway closure exists.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 6th ed. Philadelphia: Butterworth-Heinemann; 2005:34, 44.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:368, 377.

Rehder K, Marsh HM, Rodarte JR, et al. Airway closure. *Anesthesiology*. 1977;47:40.

B.7. What are the effects of anesthesia on FRC and CC?

During anesthesia, FRC is reduced by approximately 20% with spontaneous breathing and by approximately 16% with artificial ventilation. This is due to changes in the chest wall shape and diaphragm position. After induction of general anesthesia, a reduction occurs in the cross-sectional area of the rib cage corresponding to a decrease in lung volume of approximately 200 mL. Recent studies have consistently shown a cephalad movement of the dependent regions of the diaphragm, with little or no movement of the nondependent regions. However, the change in FRC that can be ascribed to changes in diaphragm is on average less than 30 mL.

CC was previously reported to be unchanged during anesthesia, but later studies concluded that CC reduced in parallel to FRC during anesthesia.

Bergman NA, Tien YK. Contribution of the closure of pulmonary units to impaired oxygenation during anesthesia. *Anesthesiology*. 1983;59:395.

Gilmour I, Burnham M, Craig DB. Closing capacity measurements during general anesthesia. *Anesthesiology*. 1976;45:477.

Juno P, Marsh HM, Knopp TJ, et al. Closing capacity in awake and anesthetized-paralyzed man. *J Appl Physiol*. 1978;44:238.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 6th ed. Philadelphia: Butterworth-Heinemann; 2005:304.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:377.

Wahba RWM. Perioperative functional residual capacity. *Can J Anaesth*. 1991;38:384–400.

B.8. Why is the FRC important in oxygenation?

First, when FRC is decreased to below CC, airways close in the dependent parts of the lung during certain periods of normal tidal ventilation. Airway closure results in shunting of pulmonary blood flow through the unventilated alveoli. Therefore, $\dot{Q}s/\dot{Q}T$ is increased and arterial oxygenation is decreased. Second, pulmonary circulation and alveolar gas exchange are continuous during both inspiratory and expiratory phases of respiration. Irrespective of whether there is airway closure, blood oxygenation during the expiratory phase depends mainly on the remaining lung volume, which is FRC. Therefore, when the FRC is high, blood oxygenation is better and there is more time for oxygenation before hypoxemia occurs during apnea. FRC is decreased in the supine position during general anesthesia and in patients with acute respiratory distress syndrome. Positive end-expiratory pressure increases FRC and decreases airway closure.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 6th ed. Philadelphia: Butterworth-Heinemann; 2005:34, 44.

B.9. Are there methods to measure FRC and CV?

FRC may be measured by helium dilution, nitrogen washout, and body plethysmography. CV may be determined by two techniques, the single-breath nitrogen test (residual gas technique) and the bolus technique with an inert tracer gas such as helium, xenon, or argon.

Buist AS. The single-breath nitrogen test. *N Engl J Med*. 1975;293:438.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 6th ed. Philadelphia: Butterworth-Heinemann; 2005:36–37, 52–53.

B.10. Give the equations for shunt (Q_S/Q_T) and dead space/tidal volume (V_D/V_T). What are their normal values?

$$Q_S/Q_T = \frac{Cc\overline{O}_2 - CaO_2}{Cc\overline{O}_2 - C\bar{v}O_2} \qquad V_D/V_T = \frac{Paco_2 - P\bar{E}co_2}{Paco_2}$$

where $Cc\overline{O}_2$, CaO_2, and $C\bar{v}O_2$ are oxygen contents in pulmonary capillary, arterial, and mixed venous blood, respectively; Q_T is cardiac output; Q_S is shunt blood; and $Paco_2$ and $P\bar{E}co_2$ are partial pressures of CO_2 in arterial blood and the mixed expired gases, respectively.

Normal Q_S/Q_T is 4% to 5%, and V_D/V_T is approximately 0.3.

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:246–247.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 6th ed. Philadelphia: Butterworth-Heinemann; 2005:33–35.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:375, 385.

B.11. Interpret the following ABGs: pH, 7.36; P_{CO_2}, 60 mm Hg; P_{O_2}, 70 mm Hg; CO_2 content, 36 mEq per L.

The fraction of inspired oxygen (F_{IO_2}) is essential to evaluate Pao_2. Assume the blood sample is obtained while the patient is breathing room air. The blood gases show mild hypoxemia and respiratory acidosis, compensated by metabolic alkalosis. The blood gases are compatible with COPD.

B.12. What are the common physiologic causes of hypoxemia?

From the shunt equation, arterial oxygen content is related to the change in pulmonary capillary oxygen content, venous oxygen content, and venous admixture. It is easier to classify hypoxemia into the following three categories.

Decreased pulmonary capillary oxygen tension

- Hypoventilation
- Low F_{IO_2}
- Ventilation/perfusion mismatch from pulmonary parenchymal change
- Diffusion abnormality (rare)

Increased shunting

- Either intrapulmonary or cardiac

Reduced venous oxygen content

- Congestive heart failure—low cardiac output
- Increased metabolism—fever, hyperthyroidism, shivering
- Decreased arterial oxygen content—anemia

Fauci AS, Braunwald E, Kasper Malley WJ. *Clinical Blood Gases, Assessment and Intervention.* 2nd ed. St. Louis: Saunders; 2005:236–239.

Miller RD, ed. *Miller's Anesthesia.* 7th ed. Philadelphia: Churchill Livingstone; 2010:373–374.

B.13. Would you order any special preoperative preparations for asthmatic patients with COPD?

Yes. The preoperative preparation should include the following:

- Eradication of acute and chronic infection with appropriate antibiotics
- Relief of bronchial spasm with a bronchodilator
- Chest physiotherapy to improve sputum clearance and bronchial drainage
- Reversal of uncompensated or borderline cor pulmonale with diuretics, digitalis, improved oxygenation, and correction of acidemia by more efficient ventilation
- Correction of dehydration and electrolyte imbalance
- Familiarization with respiratory therapy equipment likely to be used in the postoperative period
- Cessation of smoking, if possible for 2 months, to improve mucociliary clearance and decrease sputum production
- Abstinence from smoking for 2 days (at least 12 hours), to reduce carboxyhemoglobin levels, resulting in improvement of blood oxygen content and increasing the release of oxygen in hemoglobin
- Continuation of anti-inflammatory and bronchodilator therapy up to the time of surgery
- Initiation of steroid therapy with oral methylprednisolone 40 mg for 5 days before elective surgery for patients with newly diagnosed disease, poorly compliant patients, and patients with ongoing wheezing

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia.* 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1036.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone; 2008:163–173.

Miller RD, ed. *Miller's Anesthesia.* 7th ed. Philadelphia: Churchill Livingstone; 2010: 1103–1104, 1022.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth.* 2009;103(suppl l):i57–i65.

B.14. How long would you postpone elective surgery if the patient had a recent upper respiratory infection (URI)?

Respiratory tract infections are the most common stimuli that evoke acute exacerbations of asthma. The airway responsiveness of even healthy subjects to nonspecific stimuli is transiently increased after a viral infection. It is unclear how long surgery should be delayed following a URI because airway hyperreactivity can last 2 to

8 weeks after the infection in both healthy subjects and patients with asthma. Cohen and Cameron reported that if a child had a URI and had endotracheal anesthesia, the risk of a respiratory complication increased 11-fold. In addition, Tait and Knight found that laryngospasm and bronchospasm were significantly increased even in healthy children 2 weeks after a URI. Therefore, the recommendation is to wait 2 to 3 weeks after clinical recovery from a URI in patients with asthma even if clinical symptoms are not present. Nevertheless, a frequently cited retrospective study by Warner et al. found no increase in incidence of intraoperative bronchospasm in the patients with asthma who have had a recent URI.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1208.

Cohen MM, Cameron CB. Should you cancel the operation when a child has an upper respiratory infection? *Anesth Analg*. 1991;72:282–288.

Tait AR, Knight PR. Intraoperative respiratory complications in patients with upper respiratory tract infections. *Can J Anaesth*. 1987;34:300–303.

Warner DO, Warner MA, Barnes RD, et al. Perioperative respiratory complications in patients with asthma. *Anesthesiology*. 1996;85:460–467.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl l):i57–i65.

B.15. What medicines would you expect the patient to have taken in the past or to be taking at the present time?

The main drugs for asthma can be divided into bronchodilators, which are for rapid relief of bronchoconstriction, and controllers, which inhibit the underlying inflammatory process. There are three bronchodilators in current use: β_2-agonists, anticholinergics, and theophylline; of these, β_2-agonists are the most effective. Inhaled corticosteroids are by far the most effective controllers for asthma, and their early use has revolutionized asthma therapy. Special attention is required if the patient has taken systemic corticosteroids. Recently, aerosol therapy has become quite popular because it provides optimal local therapeutic effects and minimizes the systemic side effects. Various relatively selective β_2-agonists (albuterol, fenoterol, terbutaline, and bitolterol), anticholinergic bronchodilators (ipratropium bromide and methylatropine nitrate), a mast cell stabilizer (cromolyn), leukotriene receptor antagonists such as zafirlukast (Accolate) and montelukast (Singulair), and various corticosteroids are now available as aerosols and are able to control most cases of chronic asthma.

Fanta CH. Asthma. *N Engl J Med*. 2009;360:1002–1014.

Fauci AS, Braunwald E, Kasper DL, et al., eds. *Harrison's Principles of Internal Medicine*. 17th ed. New York: McGraw-Hill; 2008:1596–1607.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone; 2008:163–173.

B.16. Would you order preoperative steroid preparation? Why?

It is recommended that preoperative corticosteroid replacement therapy be given to all patients with known or suspected adrenal insufficiency. Patients who have been treated with systemic steroids for more than 2 weeks within the previous 6 months should also be assumed to have an unknown element of adrenocortical suppression that should be treated with full replacement therapy for major stress or surgery. The

human adrenal glands normally secrete approximately 30 mg of hydrocortisone (cortisol) per day under baseline conditions; nevertheless, under stress up to 200 to 500 mg per day may be secreted. It is reasonable to replace 300 mg of hydrocortisone per day during perioperative periods. A 100-mg dose of hydrocortisone phosphate is given intravenously before induction and during surgery. Postoperatively, hydrocortisone phosphate 100 mg intravenously is given every 8 hours for 48 hours. The biologic half-life of hydrocortisone is 8 to 12 hours. If the patient received less than 1 week of systemic steroid therapy more than 6 months previously and there are no signs of adrenal insufficiency, routine steroid preparation is not advised. However, intravenous steroid preparations should be available in the operating room in case intractable hypotension from adrenal insufficiency occurs during surgery.

The increasing emphasis on reactive airways as an inflammatory disease has led to greater appreciation of the importance of steroids in controlling the incidence of attacks and in aborting acute attacks. It has been recommended that systemic steroid preparation be used preoperatively in patients with moderate to severe asthma and a history of a need for systemic steroids in the past. One day of high-dose steroids should not significantly affect wound healing. In the face of ongoing wheezing and scheduled elective surgery, oral methylprednisolone 40 mg daily for 5 days before surgery has been shown to decrease postintubation bronchospasm. The concern that steroids will increase the rate of wound-healing problems or infection is not well founded. A study of patients with asthma treated with steroids preoperatively found no increase in the incidence of wound infections or wound-healing problems.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:582.

Bishop MJ. Editorial views: preoperative corticosteroids for reactive airway. *Anesthesiology*. 2004;100:1047–1048.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone; 2008:163–173.

Kabalin CS, Yarnold PR, Grammer LC. Low complication rate of corticosteroid-treated asthmatics undergoing surgical procedures. *Arch Intern Med*. 1995;155:1379–1384.

Silvanus M-T, Groeben H, Peters J. Corticosteroids and inhaled salbutamol in patients with reversible airway obstruction markedly decrease the incidence of bronchospasm after tracheal intubation. *Anesthesiology*. 2004;100:1052–1057.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl l):i57–i65.

B.17. What is the onset of action of intravenous steroid therapy in asthma?

The bronchial effects of intravenous steroids are not immediate and may not be seen for 4 to 6 hours after initial administration. When severe bronchospasm does not resolve despite intense optimal bronchodilator therapy, intravenous corticosteroid administration is indicated. A loading dose of hydrocortisone 4 mg per kg is given to achieve plasma cortisol levels above 100 μg per dL, followed by 3 mg per kg every 6 hours. Alternatively, methylprednisolone, 125 mg, may be given every 6 hours.

Fauci AS, Braunwald E, Kasper DL, et al., eds. *Harrison's Principles of Internal Medicine*. 17th ed. New York: McGraw-Hill; 2008:1596–1607.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone; 2008:163–173.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl l):i57–i65.

B.18. What are the effects of H_2-receptor antagonists on patients with asthma?

Nathan et al. found that histamine mediates bronchoconstriction through the H_1-receptor (blocked by chlorpheniramine) and bronchodilation is mediated by H_2-receptor agonists (blocked by cimetidine). H_2-receptors are thought to be responsible for inhibitory feedback control of mediator release. Cimetidine may potentiate histamine H_1-receptor bronchoconstriction. It should be avoided in asthmatic patients. H_2-receptor antagonists also slow clearing of theophylline by inhibiting microsomal metabolism. Therefore, theophylline dosage should be decreased to avoid toxicity.

Nathan R, Segall N, Schocket A. A comparison of the actions of H_1 and H_2 antihistamines on histamine-induced bronchoconstriction and cutaneous wheal response in asthmatic patients. *J Allergy Clin Immunol*. 1981;67:171.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and co-existing disease*. 5th ed. Philadelphia: Churchill Livingstone, 2008:163–173.

B.19. How would you premedicate the patient? Why?

Inhaled or systemic steroids may be given to patients with moderate-to-severe asthma to decrease the incidence of asthmatic attacks. Anti-inflammatory and bronchodilator therapy should be continued up to the time of surgery.

No good controlled studies have been performed on premedication used in patients with asthma. The patient with asthma may be premedicated with atropine and diphenhydramine. Atropine is an anticholinergic drug. It decreases airway resistance and diminishes secretion-initiated airway reactivity. Diphenhydramine is an H_1-receptor–blocking drug. It inhibits histamine-mediated bronchoconstriction and possesses a sedative effect. The sedative effect of diphenhydramine may prevent bronchospasm induced by psychological stress. Hydroxyzine hydrochloride (Vistaril) is a frequently used alternative because of its sedative, antihistaminic, and bronchodilating effects.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone; 2008:163–173.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl l):i57–i65.

C. Intraoperative Management

C.1. What are the disadvantages of administering atropine to the patient with asthma?

Some physicians consider atropine relatively contraindicated because it causes drying of secretions, further plugging, and perhaps initiation of a severe attack of asthma. This assumption has proved more theoretic than real in the reasonably well-managed asthmatic patient. Moreover, atropine blocks the formation of cyclic guanosine monophosphate and therefore has a bronchodilation effect. Inhaled atropine improves FEV_1 in 85% of patients with COPD.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:592.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone; 2008:163–173.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth.* 2009;103(suppl l):i57–i65.

C.2. If the patient had a severe asthmatic attack in the operating room before the induction of anesthesia, would you proceed with the anesthetic or postpone the surgery?

First, medical treatment should be given to relieve the asthmatic attack. Elective surgery should be postponed, and the patient should be reevaluated carefully and better prepared preoperatively. In the case of emergency surgery, such as acute appendicitis, the surgery can be performed after the asthmatic attack is successfully treated. Regional anesthesia, if feasible, should be considered. During surgery, the medical treatment should be continued.

C.3. The patient did not have an asthmatic attack in the operating room. How would you induce anesthesia? Would you use a laryngeal mask airway (LMA) instead of an endotracheal tube?

The principles of anesthetic management for the asthmatic patient are threefold: to block airway reflexes before laryngoscopy and intubation, to relax airway smooth muscle, and to prevent release of biochemical mediators. Before induction of anesthesia, I like to ask the patient to take two or three puffs of albuterol from a metered-dose inhaler (MDI). Propofol 2.5 mg per kg is used for induction. Then oxygen and a potent inhalation agent, such as halothane or sevoflurane, are administered by mask to achieve adequate depth of anesthesia that suppresses hyperreactive airway reflexes sufficiently to permit tracheal intubation without triggering bronchospasm. The lesser pungency of sevoflurane and halothane (compared with desflurane and isoflurane) may decrease the likelihood of coughing, which can induce bronchospasm. Endotracheal intubation is accomplished following injection of succinylcholine or other muscle relaxants. Topical endotracheal spray of lidocaine 80 to 120 mg through a laryngotracheal anesthesia kit may be used before intubation to suppress the cough reflex induced by intubation, but the introduction of lidocaine itself may cause the cough reflex when an adequate depth of anesthesia has not been achieved.

As a supraglottic airway, the LMA seems to be suitable for patients with asthma. The LMA provides a unique opportunity for the clinician to control the airway without having to introduce a foreign body into the trachea. Therefore, it may be an ideal airway tool in the patient with asthma who is not at risk for reflux and aspiration. The patient is undergoing cholecystectomy, which may require manipulating and packing of stomach and bowels, and is at risk for regurgitation and aspiration. Meanwhile, the patient may need a nasogastric tube for gastrointestinal tract decompression. The classic LMA device (except LMA-ProSeal) is not compatible with the use of a nasogastric tube intraoperatively. I would not choose a classic LMA instead of an endotracheal tube for this procedure. Nevertheless, the introduction of the LMA-ProSeal with a gastric drain tube and larger cuff reduces both the risk for gastric inflation and aspiration of refluxed gastric contents. The LMA-ProSeal has been successfully used for laparoscopic cholecystectomy in obese patients.

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:760.

Malthy JR, Beriault MT, Watson NC, et al. The LMA ProSeal is an effective alternative to tracheal intubation in laparoscopic cholecystectomy. *Can J Anaesth.* 2002;49:857.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth.* 2009;103(suppl l):i57–i65.

C.4. Why would you use propofol for induction of anesthesia?

Propofol may be the induction agent of choice for the patient with reactive airways who is hemodynamically stable. A recent report found that induction of patients with asthma with propofol 2.5 mg per kg of body weight resulted in a significantly lower incidence of wheezing after tracheal intubation compared with induction of thiopental or thiamylal 5 mg per kg or methohexital 1.75 mg per kg of body weight. The incidence of wheezing was 0%, 45%, and 26% in patients who received propofol, a thiobarbiturate, and oxybarbiturate, respectively. Another study found that in unselected patients, propofol resulted in a significantly lower respiratory resistance after tracheal intubation than induction with thiopental or etomidate. Nevertheless, propofol-induced bronchospasm has been reported in patients with allergic rhinitis. Therefore, propofol should be used with caution in patients who are allergic.

Eames WO, Rooke GA, Wu RS, et al. Comparison of the effects of etomidate, propofol, and thiopental on respiratory resistance following tracheal intubation. *Anesthesiology.* 1996;84:1307–1311.

Nishiyama T, Hanaoka K. Propofol-induced bronchoconstriction: two case reports. *Anesth Analg.* 2001;93:645–646.

Pizov R, Brown RH, Weis YS, et al. Wheezing during induction of general anesthesia in patients with and without asthma: a randomized, blind trial. *Anesthesiology.* 1995;82:1111–1116.

C.5. Would you use thiopental, methohexital, etomidate, or ketamine for induction?

Thiopental and thiamylal, but not methohexital and pentobarbital, have been demonstrated to release histamine. Thiopental and thiamylal are thiobarbiturates, and methohexital and pentobarbital are oxybarbiturates. This suggests that the sulfur atom is important in barbiturate-induced histamine release. Moreover, they further found that thiobarbiturates, but not oxybarbiturates, constricted guinea pig tracheas and that this constriction was mediated by thromboxane. Therefore, methohexital may be preferred as the induction agent in patients showing extreme sensitivity to histamine (asthmatics) or increased histamine releasability (atopics). Nevertheless, thiopental does not cause bronchospasm. Because it provides only a light plane of anesthesia, airway instrumentation under thiopental anesthesia alone may trigger bronchospasm. Therefore, clinically, both barbiturates have been used successfully in patients with asthma, provided that an adequate depth of anesthesia is achieved before stimulating the airway.

Etomidate does not depress myocardial function and therefore provides hemodynamic stability in critically ill patients. Although it was advertised as an ideal agent for patients with asthma, little evidence supports the claim except that etomidate does not release histamine. A study suggests that neither etomidate nor thiopental prevents wheezing after intubation, as opposed to the marked protection afforded by propofol.

Ketamine produces bronchodilation both through neural mechanisms and through release of catecholamines. In an actively wheezing patient, ketamine is the induction agent of choice, particularly when hemodynamics are unstable.

Bishop MJ. Bronchospasm: successful management. In: *ASA Annual Meeting Refresher Course Lectures.* Park Ridge, IL: American Society of Anesthesiologists; 2005:408.

Eames WO, Rooke GA, Wu RS, et al. Comparison of the effects of etomidate, propofol, and thiopental on respiratory resistance following tracheal intubation. *Anesthesiology*. 1996;84:1307–1311.

Curry C, Lenox WC, Spannhake EW, et al. Contractile responses of guinea pig trachea to oxybarbiturates and thiobarbiturates. *Anesthesiology*. 1991;75:679–683.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone; 2008:163–173.

Hirshman CA, Edelstein RA, Ebertz JM, et al. Thiobarbiturate-induced histamine release. *Anesthesiology*. 1985;63:353.

C.6. Would you use lidocaine for intubation?

Intravenous lidocaine 1 mg per kg has been given 1 to 2 minutes before intubation to prevent reflex-induced bronchospasm. Topical endotracheal spray of lidocaine must be used cautiously because it may provoke reflex bronchoconstriction if adequate depth of anesthesia has not been achieved. Lidocaine infusion 1 to 2 mg/kg/hr may be used in cardiac or elderly patients with COPD whose airways need more anesthesia than their cardiovascular system can tolerate.

Although intravenous lidocaine can attenuate reflex-induced bronchospasm, recent clinical studies suggested that it may cause paradoxical bronchospasm in patients with asthma. Therefore, intravenous lidocaine should be administered with caution in these patients.

Burches BR Jr, Warner DO. Bronchospasm after intravenous lidocaine. *Anesth Analg*. 2008;107:1260–1262.

Maslow AD, Regan MM, Israel E, et al. Inhaled albuterol, but not intravenous lidocaine, protects against intubation-induced bronchoconstriction in asthma. *Anesthesiology*. 2000;93:1198–1204.

McAlpine LG, Thomson NC. Lidocaine-induced bronchoconstriction in asthmatic patients: relation to histamine airway responsiveness and effect of preservative. *Chest*. 1989;96:1012–1015.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl l):i57–i65.

C.7. If this is an emergency surgery and rapid sequence induction is indicated, how would you induce anesthesia in this patient?

All precautions to prevent aspiration of gastric contents and asthmatic attack must be considered simultaneously. Rapid sequence induction and tracheal intubation using propofol, or methohexital, and succinylcholine are necessary to prevent aspiration, but light anesthesia may precipitate severe bronchospasm.

Ketamine 2 mg per kg may be the induction agent of choice in patients without cardiac disease who have asthma, because ketamine increases catecholamine release with resultant bronchodilation.

In patients with asthma who have ischemic heart disease, we give a moderate dose of fentanyl 5 μg per kg 2 to 3 minutes before the administration of propofol 1.5 mg per kg or methohexital 1.5 mg per kg to suppress airway reflexes and prevent tachycardia and hypertension caused by intubation.

Intravenous lidocaine, 1 to 2 mg per kg given immediately before the administration of ketamine or fentanyl, and succinylcholine are useful adjunct drugs to prevent reflex bronchospasm, particularly in an emergency situation when deep anesthesia cannot be achieved before intubation.

A full stomach should be emptied by a functioning nasogastric tube. The patient should be denitrogenated with 100% oxygen by mask. Cisatracurium or vecuronium 1 mg should be given 3 minutes before administration of succinylcholine.

If the patient has a wheezing attack before anesthesia, inhalation of β_2-agonists such as albuterol may be used as the first-line therapy for acute asthmatic attacks.

Martin DE, Rosenberg H, Aukburg SJ, et al. Low-dose fentanyl blunts circulatory responses to tracheal intubation. *Anesth Analg*. 1982;61:680.

C.8. What is your choice of agents for maintenance of anesthesia? Why?

We use inhalation agents such as sevoflurane, halothane, and isoflurane with nitrous oxide and oxygen. Sevoflurane, enflurane, and isoflurane are preferable to halothane, because halothane sensitizes the myocardium to arrhythmic effects of circulating catecholamines more than sevoflurane, enflurane, and isoflurane. However, some authorities prefer halothane and sevoflurane to isoflurane and desflurane because the latter anesthetics have a pungent odor that may cause airway irritation and trigger bronchospasm. At lower doses (<1.0 minimum alveolar concentration), the inhaled anesthetics inhibit chemically induced tracheal contractions in the order: *halothane* > *enflurane* ≥ *isoflurane* > *sevoflurane*. More recent clinical observations in humans indicate that sevoflurane at 1.1 minimum alveolar concentration may be the most effective agent, particularly in the presence of airway instrumentation. In addition, sevoflurane may have a more rapid onset of bronchodilation than isoflurane or halothane.

Desflurane has been shown to cause elevations in airway resistance and tissue mechanical parameters, with markedly enhanced airway narrowing in children with asthma or a recent URI. Therefore, desflurane should be avoided in children with susceptible airways.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone; 2008:163–173.

Rock GA, Choi JH, Bishop MJ. The effect of isoflurane, halothane, sevoflurane and thiopental nitrous oxide on respiratory system resistance after tracheal intubation. *Anesthesiology*. 1997;86:1294–1299.

Von Ungern-Sternberg BS, Saudan S, Petak F, et al. Desflurane but not sevoflurane impairs airway and respiratory tissue mechanics in children with susceptible airways. *Anesthesiology*. 2008;108:216–224.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl l):i57–i65.

C.9. What are the mechanisms of volatile anesthetics that produce bronchodilation?

The volatile anesthetics relax airway smooth muscle primarily by directly depressing smooth muscle contractility. This action appears to result from direct effects on bronchial epithelium and airway smooth muscle cells and indirect inhibition of the reflex neural pathways. The mechanisms responsible for the direct relaxation effects involve decreases in intracellular calcium, an important regulator of smooth muscle reactivity. Several intracellular mediators responsible for mobilization of calcium ions are potential sites for the action of volatile anesthetics, but the predominant mechanism appears to be inhibition of cell membrane–associated voltage-dependent calcium channels, an action that decreases entry of calcium ions into the cytosol. Volatile anesthetic–induced increases in cyclic 3′,5′ adenosine monophosphate (cAMP) cause decreases

in free intracellular calcium by stimulating efflux of calcium and increasing uptake of calcium into the sarcoplasmic reticulum. This action contributes to airway smooth muscle relaxation. In addition, volatile anesthetics reduce calcium sensitivity as a result of inhibition of protein kinase C activity and inhibition of G protein function.

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:434.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:563–567.

C.10. Why would you choose an inhalational instead of an intravenous technique?

First, inhalation agents such as sevoflurane, halothane, enflurane, and isoflurane have dose-related direct bronchodilator effects. Ketamine has an indirect bronchodilator effect, which is not dose related and not predictable. Large doses of morphine produce bronchoconstriction because morphine increases central vagal tone and also releases histamine. Droperidol has an α-blocking effect that may relieve bronchospasm induced by α stimulation. Meperidine was shown to have a spasmolytic effect in patients with asthma but not in experimental dogs. Fentanyl does not have a significant effect on bronchial tone.

Second, cholinesterase inhibitors can induce bronchospasm. Inhalation agents potentiate muscle relaxants; therefore, lower doses of relaxants are needed for surgery. The use of cholinesterase inhibitors to reverse the effect of muscle relaxants may be avoided or decreased.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl l):i57–i65.

C.11. Is regional anesthesia better than general anesthesia in this situation?

This issue is controversial. The use of regional anesthesia avoids the possibility of bronchospasm that may be induced by endotracheal tube stimulation. Nevertheless, if high levels of sensory and motor block are required, they may produce severe anxiety and actually incite bronchospasm. Another concern is the associated blockade of sympathetic input to the lungs. Some case reports have speculated about a resultant increase in airway resistance. Respiratory complications were reported to be quite common (83%) in patients undergoing intraperitoneal surgery who had relatively high spinal anesthesia (T6–4). Low spinal, epidural, and caudal anesthesia for surgery of the perineum, lower extremities, and pelvic extraperitoneal organs resulted in fewer respiratory complications than did general anesthesia. A study of patients with asthma demonstrated no differences between those anesthetized with high epidurals (T2–4) and those undergoing general anesthesia with ketamine and isoflurane.

Endotracheal general anesthesia is advantageous because it provides a controlled airway to deliver the desirable oxygen concentration, but the endotracheal tube may also induce bronchospasm during light anesthesia.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone; 2008:163–173.

Ramanathan J, Osborne B, Sibai B. Epidural anesthesia in asthmatic patients. *Anesth Analg*. 1990;70:S317–S318.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl l):i57–i65.

C.12. Which muscle relaxants would you use? Why?

Muscle relaxants that cause histamine release should be avoided (Table 1.2). Rocuronium, cisatracurium, and vecuronium are the preferred relaxants because the histamine released is insignificant. Vecuronium, rocuronium, and cisatracurium may be better choices of relaxants because of their intermediate action durations, allowing early recovery without reversal with an anticholinesterase, which may precipitate bronchospasm. D-Tubocurarine can cause bronchospasm by histamine release. Metocurine and succinylcholine also cause histamine release but to a lesser extent. There is no evidence that succinylcholine is associated with increased airway resistance in patients with asthma. Gallamine has minimal histamine release but has been reported to cause bronchospasm. Atracurium, mivacurium, and doxacurium in high doses increase histamine release. Therefore, they are not the relaxants of choice.

Basta SJ. Modulation of histamine release by neuromuscular blocking drugs. *Curr Opin Anesth.* 1992;5:572.

Caldwell JE, Lau M, Fisher DM. Atracurium versus vecuronium in asthmatic patients: a blinded, randomized comparison of adverse events. *Anesthesiology.* 1995;83:985–991.

Mehr EH, Hirshman CA, Lindeman KS. Mechanism of action of atracurium on airways. *Anesthesiology.* 1992;76:448–454.

Miller RD, ed. *Miller's Anesthesia.* 7th ed. Philadelphia: Churchill Livingstone; 2010:882–890.

C.13. In the middle of surgery, the patient developed a severe wheezing attack. How do you manage it?

First, deepen the level of anesthesia and increase F_{IO_2}. Remember that the patient is under anesthesia and undergoing surgery. Therefore, medical intervention, such as β-agonist administration, is not the first choice of treatment. The most common cause of asthmatic attack during surgery is inadequate depth of anesthesia. The patient with asthma has an extremely sensitive tracheobronchial tree. When the level of anesthesia is too light, the patient may develop bucking, straining, or coughing as a result of the foreign body (endotracheal tube) in the trachea and then bronchospasm. First, the blood pressure is taken to ensure it is normal or high, and then anesthesia is deepened by increasing the concentration of inhalation agents, such as sevoflurane, halothane, or isoflurane, which are direct bronchodilators as well. An incremental dose of ketamine may be a quick way of maintaining blood pressure, rapidly deepening anesthesia, achieving bronchodilation, and avoiding the problem of delivering an inhaled anesthetic to a patient with poor ventilation. At the same time, oxygenation can be improved by increasing the inspired oxygen concentration and decreasing nitrous oxide. The patient should be continuously ventilated with a volume-cycled ventilator.

Second, relieve mechanical stimulation. Pass a catheter through the endotracheal tube to suction secretions and determine whether there is an obstruction, kinking of the tube, or overinflation of the endotracheal tube cuff. The cuff of the endotracheal tube can be deflated, the tube moved back 1 to 2 cm, and the cuff reinflated. Occasionally, the endotracheal tube slips down and stimulates the carina of the trachea, causing severe bronchospasm during light anesthesia. Surgical stimulation, such as traction on the mesentery, intestine, or stomach, should be stopped temporarily, because it causes vagal reflex and can cause bronchospasm.

Third, medical intervention is necessary if the previously mentioned treatment cannot break the bronchospasm or the anesthesia cannot be increased because of hypotension. The cornerstone of the treatment of the intraoperative bronchospasm is inhalation of β_2-agonists such as albuterol, which induce further bronchodilation even

Table 1.2 Histamine Release from Nondepolarizing Muscle Relaxants

MUSCLE RELAXANT	HISTAMINE RELEASE[a]
Benzylisoquinolinium compounds	
D-Tubocurarine	0.6
Metocurine	2.0
Doxacurium	>4.0
Mivacurium	3.0
Atracurium	2.5
Cisatracurium	None
Steroidal compounds	
Pancuronium	None
Vecuronium	None
Pipecuronium	None
Rocuronium	None
Others	
Alcuronium	None
Gallamine	None

[a] Defined as the number of multiples of the ED_{95} for neuromuscular blockade required to produce histamine release.

in the presence of adequate inhalational anesthesia. Because of rain-out in the endotracheal tube, a considerably larger dose (8–10 puffs) should be given to achieve adequate therapeutic levels. When severe bronchospasm is not resolving despite intense optimal bronchodilation therapy, high-dose intravenous corticosteroids are indicated (see sections B.16 and B.17). If bronchospasm remains refractory, epinephrine 5 to 10 μg can be given intravenously, although this has a high risk of exacerbating tachycardia and tachyarrhythmias. Alternatively, a continuous infusion of epinephrine 0.5 to 2 μg per minute in adults can provide maintenance bronchodilation with fewer adverse effects.

Fourth, bring in an intensive care unit (ICU) ventilator. Anesthesia ventilators are not designed for patients with high airway resistance. It is impossible to deliver adequate alveolar ventilation because the anesthesia circuit has too much compressible volume (tubing compliance) and the anesthesia ventilator does not have sufficient driving power. An ICU ventilator can generate inspiratory pressures as high as 120 cm H_2O. With low tubing compliance, little ventilation is wasted into the circuit. A high inspiratory flow rate allows for shorter inspiratory time with adequate time for expiration and lower auto-positive end-expiratory pressure. The major disadvantage of an ICU ventilator is its inability to use inhalational anesthetics. However, the Siemens 900D anesthesia machine incorporates an ICU-type ventilator with vaporizers and oxygen mixers. It may be ideal for this situation.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease.* 5th ed. Philadelphia: Churchill Livingstone; 2008:163–173.

Tobias JD, Hirshman CA. Attenuation of histamine-induced airway constriction by albuterol during halothane anesthesia. *Anesthesiology.* 1990;72:105–110.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth.* 2009;103(suppl l):i57–i65.

C.14. How would you give β_2-agonists? What is their mechanism of action on asthma?

In the past, it was fashionable to treat episodes of severe asthma with intravenous sympathomimetics such as isoproterenol. This approach no longer appears justifiable. Isoproterenol infusions can induce ventricular arrhythmias during halothane anesthesia. In addition, isoproterenol infusion can clearly cause myocardial damage, and even the β_2-selective agents such as terbutaline and albuterol when given intravenously offer no advantages over the inhaled route.

β_2-agonists such as albuterol, terbutaline, fenoterol, and pirbuterol may be administered through MDI adapters or small-volume jet nebulizers to the anesthetic circuit. Because MDI adapters are not very efficient in the intubated patient, 8 to 10 puffs are needed to break acute bronchospasms.

Adrenergic stimulants produce bronchodilation through action on β-adrenergic receptors. β-agonists increase intracellular cAMP by activating adenyl cyclase, which produces cAMP from adenosine triphosphate. Increased cAMP promotes bronchial relaxation and inhibits the release of mediators from mast cells (Fig. 1.6).

Fanta CH. Asthma. *N Engl J Med.* 2009;360:1002–1014.

Fauci AS, Braunwald E, Kasper DL, et al., eds. *Harrison's Principles of Internal Medicine*. 17th ed. New York: McGraw-Hill; 2008:1596–1607.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone; 2008:163–173.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth.* 2009;103(suppl l):i57–i65.

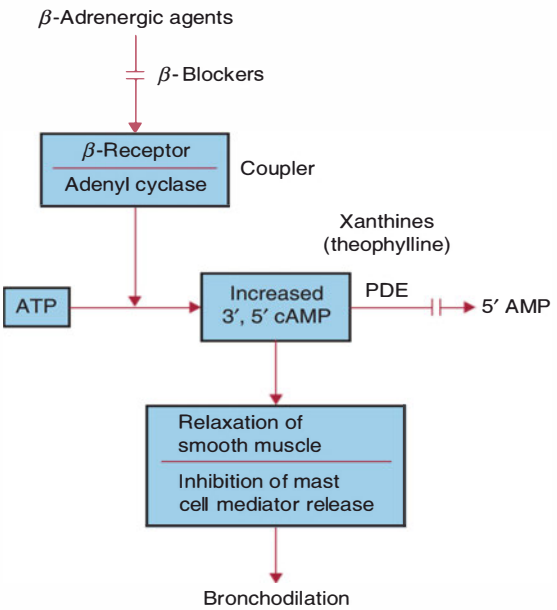

Figure 1.6 Cyclic adenosine monophosphate (cAMP) pathways involved in bronchodilator action. 3′,5′, cAMP, cyclic 3′, 5′ adenosine monophosphate; AMP, adenosine monophosphate; ATP, adenosine triphosphate; PDE, phosphodiesterase. (From Hirshman C. Airway reactivity in humans: anesthetic implications. Anesthesiology. 1983;58:170, with permission.)

C.15. Would you administer aminophylline? How does aminophylline relieve bronchospasm? What is the mechanism of action? What are the toxic effects of aminophylline?

Currently, aminophylline is rarely used for acute bronchospasm because of its narrow therapeutic–toxic window and its relatively weak bronchodilating effect. In addition, aminophylline does not add to the bronchodilating efficacy of inhaled anesthetics.

It was formerly thought that aminophylline increases intracellular cAMP through inhibition of the enzyme phosphodiesterase, which inactivates cAMP (Fig. 1.6). However, the available evidence does not support this concept. There is increasing evidence that theophylline at lower doses has anti-inflammatory effects, which are likely mediated through different molecular mechanisms. Theophylline activates the key nuclear enzyme histone deacetylase-2, which is a critical mechanism for switching off activated inflammatory genes. The common side effects of aminophylline include nervousness, nausea, vomiting, anorexia, and headache; cardiac arrhythmias and seizures occur with high plasma levels.

Fauci AS, Braunwald E, Kasper DL, et al., eds. *Harrison's Principles of Internal Medicine*. 17th ed. New York: McGraw-Hill; 2008:1596–1607.

Tobias JD, Kubos KL, Hirshman CA. Aminophylline does not attenuate histamine-induced airway constriction during halothane anesthesia. *Anesthesiology*. 1989;71:723–729.

C.16. If the patient does not respond to the aforementioned treatment and becomes cyanotic, what would you do?

The ABG values should be determined immediately. In a severe, prolonged asthmatic attack, there will be combined respiratory and metabolic acidosis resulting from CO_2 retention and lactic acidosis from tissue hypoxia. Hypercarbia, hypoxemia, and acidemia promote arrhythmias and impair the response to bronchodilator therapy. $NaHCO_3$ should be given to correct the acidosis, because β-agonists are not effective in severe acidosis. At the same time, bronchodilator therapy should be continued or increased. Consultation with senior staff or a physician in pulmonary medicine may be necessary.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl l):i57–i65.

C.17. What are the differential diagnoses of intraoperative bronchospasm?

The causes of wheezing and increased airway pressure include the following:

- Mechanical obstruction of endotracheal tube
  - Kinking
  - Solidified secretions or blood
  - Overinflation of tracheal tube cuff
- Inadequate depth of anesthesia
- Pulmonary edema
- Tension pneumothorax
- Aspiration pneumonitis
- Pulmonary embolism
- Endobronchial intubation
- Persistent coughing and straining
- Asthmatic attack

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone; 2008:163–173.

C.18. The asthmatic attack was finally relieved, and the surgery was completed. The patient was found to be hypoventilating. What are the common causes of hypoventilation? Would you like to reverse the muscle relaxant?

The following are common causes of apnea or hypoventilation at the end of surgery:

- Respiratory center depression by inhalational anesthetics, opioids, or mechanical hyperventilation (low $Paco_2$)
- Peripheral blockade by muscle relaxants

Because the patient has severe asthma, it is better to avoid the use of an anticholinesterase, such as neostigmine, to reverse a nondepolarizing relaxant. Neostigmine may trigger bronchospasm by cholinergic and prosecretory effects. Although atropine or glycopyrrolate given simultaneously with neostigmine may prevent bronchospasm, the action duration of neostigmine can outlast that of a vagolytic agent, especially in the presence of renal insufficiency. If reversal is required, it appears prudent to administer larger than customary doses of glycopyrrolate (>0.5 mg) or atropine (>1 mg) to minimize the possibility of bronchospasm. It is advisable to use inhalation agents to potentiate relaxants and to use smaller amounts of intermediate-acting relaxants for surgery. If spontaneous respiration is not adequate, artificial ventilation should be continued.

Hazizai A, Hatija A. Bronchospasm caused by neostigmine. *Eur J Anaesthesiol*. 2006;23:85–86.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl l):i57–i65.

D. Postoperative Management

D.1. Would you extubate the patient with asthma while he or she was deeply anesthetized?

To avoid bronchospasm triggered by coughing and bucking caused by laryngeal and pharyngeal reflexes during emergence and extubation, patients may be extubated at surgical (deep) levels of anesthesia. However, the risks of aspiration, airway obstruction, and hypoventilation should be weighed against the benefits. With a history of severe COPD, chronic hypoxemia, and CO_2 retention, the patient was not a good candidate for extubation while deeply anesthetized. A systematic approach for emergence and extubation is illustrated in Figure 1.7. However, the guidelines do not include all possible patient-surgical-anesthetic conditions. Certainly, the practitioner's clinical judgment is of utmost importance in the decision about whether to extubate the patient.

Lien CA, Koff H, Malhotra V, et al. Emergence and extubation: a systemic approach. *Anesth Analg*. 1997;85:1177.

Miller KH, Harkin CP, Bailey PL. Postoperative tracheal extubation. *Anesth Analg*. 1995;80:148–172.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl l):i57–i65.

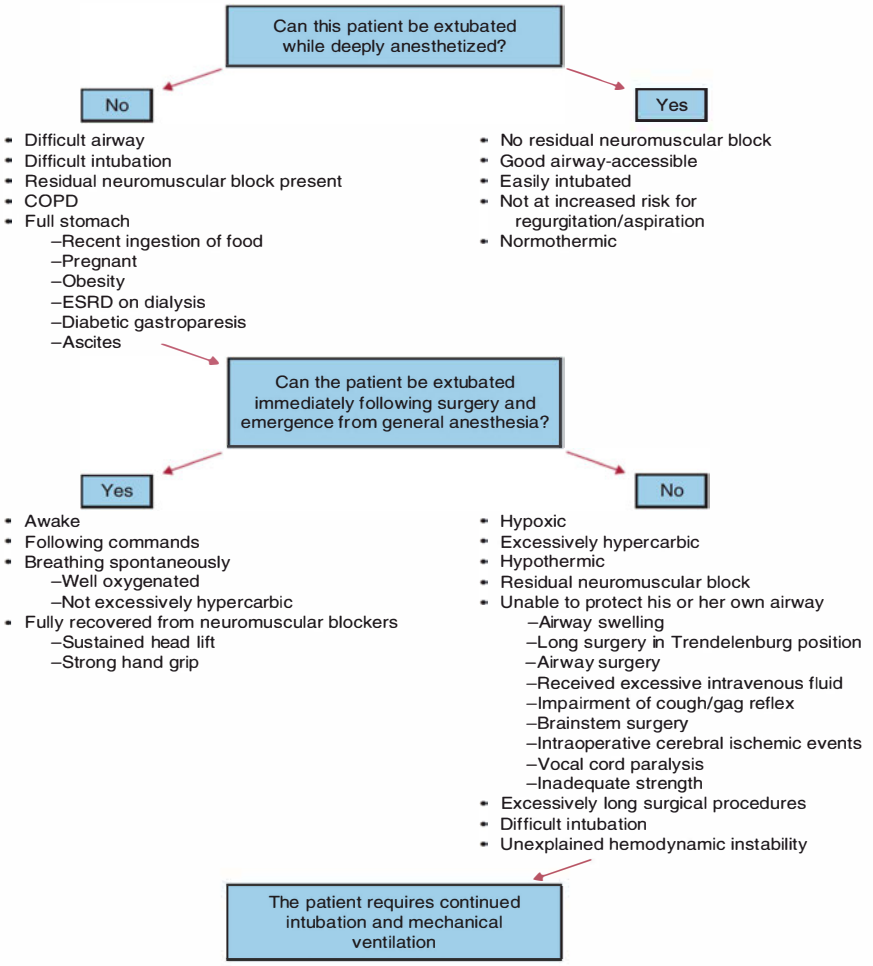

Figure 1.7 A systematic approach to emergence and extubation. COPD, chronic obstructive pulmonary disease; ESRD, end-stage renal disease.

D.2. When the patient cannot be extubated early in the recovery room, how would you keep the endotracheal tube in place without causing bronchoconstriction?

Loading doses of lidocaine, followed by continuous infusion, as described in section C.6, may be administered intravenously to prevent bronchoconstriction induced by stimulation of the endotracheal tube. β_2-agonists such as albuterol may be administered through MDI adapter to prevent bronchospasm. Alternatively, an LMA may be used to replace the endotracheal tube for control of ventilation and to avoid tracheal stimulation.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth.* 2009;103(suppl l):i57–i65.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone; 2008:163–173.

D.3. In patients with asthma, are Opioids contraindicated for postoperative pain control?

Opioids should be used very carefully because prolonged respiratory depression may further compromise the airway. Morphine is avoided because of possible histamine release and increased central vagal tone, which may cause bronchospasm. Meperidine may be a better choice for postoperative analgesia because of its spasmolytic action. Narcotics should be titrated carefully to control pain and not depress respiration. Poor pain control may compromise respiration because of splinting of the thoracic cage and decreased ability to cough. Paravertebral or intercostal nerve blocks, epidural analgesia, or transcutaneous electrical nerve stimulation may be used to control postoperative pain without depressing respiration.

NSAIDs precipitate acute bronchospasm in an estimated 8% to 20% of adult patients with asthma. NSAIDs block the cyclooxygenase-mediated conversion of arachidonic acid to prostaglandins, thereby shunting arachidonic acid toward the formation of bronchoconstrictor leukotrienes. Therefore, it may be prudent to avoid NSAIDs for postoperative pain control.

Fauci AS, Braunwald E, Kasper DL, et al., eds. *Harrison's Principles of Internal Medicine*. 17th ed. Philadelphia: McGraw-Hill; 2008:1606.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone; 2008:163–173.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:786.

D.4. The patient was breathing well and was extubated. How much oxygen would you give to this patient with asthma and COPD in the recovery room?

For a small proportion of patients with COPD, the hypoxic drive might be taken away by increased F_{IO_2}. Moreover, oxygen therapy may abolish hypoxic pulmonary vasoconstriction in poorly ventilated areas, increasing blood flow to these areas and so decreasing blood flow to other lung regions with normal or high ventilation/perfusion ratios. These regions will then contribute to alveolar dead space, causing an increase in P_{aCO_2}. It is important to monitor the patient's respiration, oxygenation, and P_{aCO_2} very carefully during oxygen therapy. Venturi masks with F_{IO_2} of 0.24 to 0.4 may be used for patients with COPD. Nevertheless, adequate oxygen concentration must be used in the presence of hypoxemia. Hypoventilation can be assisted or controlled by artificial ventilation.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 6th ed. Philadelphia: Butterworth-Heinemann; 2005:191, 381.

CHAPTER 2

Bronchoscopy, Mediastinoscopy, and Thoracotomy

Alessia Pedoto, Paul M. Heerdt, and Fun-Sun F. Yao

A 60-YEAR-OLD MAN

has suffered from cough, intermittent hemoptysis, and weight loss for 2 months. He has smoked one pack of cigarettes per day for 40 years. A chest radiograph 1 month ago revealed a right middle lobe infiltrate that was treated with antibiotics without clinical improvement. Subsequent evaluation revealed a carcinoma. He is now scheduled for fiber-optic bronchoscopy, mediastinoscopy, and possible video-assisted thoracoscopic (VATS) lobectomy.

A. Medical Disease and Differential Diagnosis

1. How is the diagnosis of lung carcinoma made? What is your prediction for the most likely type of malignancy?
2. What are the less common manifestations of bronchogenic carcinoma?
3. The patient has a long history of cigarette smoking. What is the significance of this finding?

B. Preoperative Evaluation and Preparation

1. How would you evaluate the patient preoperatively?
2. What are the pulmonary function guidelines that indicate increased risk for morbidity and mortality?

C. Intraoperative Management

1. How would you premedicate, monitor, and anesthetize this patient?
2. How many types of bronchoscopes are available and what are the intraoperative considerations of each one?
3. What are the indications for cervical mediastinoscopy? Are there potential complications?
4. The decision was made to proceed with a right VATS middle lobectomy. How would this alter your management?
5. What are the indications for single-lung ventilation and how can it be accomplished?

6. What are the contraindications to the use of double-lumen endotracheal tubes (DLTs)?
7. Would you use a right- or left-sided double-lumen tube?
8. How do you know that the tube is in the correct position?
9. How many types of bronchial blockers are available? What are the advantages and disadvantages of bronchial blockers?
10. How will systemic oxygenation be monitored during single-lung ventilation? What is the mechanism of pulse oximetry?
11. The patient was placed in the lateral decubitus position. Describe the effects of lateral positioning on pulmonary blood flow and respiration.
12. What is hypoxic pulmonary vasoconstriction (HPV)?
13. What are the effects of anesthetic agents on HPV and their clinical implications?
14. Discuss pulmonary blood flow distribution, shunt flow, and Pao_2 (F_IO_2 = 1.0) during single-lung ventilation in the lateral position.
15. How could you improve oxygenation during single-lung ventilation?
16. A right middle lobectomy was performed. Would you extubate the trachea at the end of the procedure?

D. Postoperative Management

1. What are the immediate life-threatening complications that follow lobectomy or pneumonectomy?
2. Why is it important to control postoperative pain? How would you achieve this?

A. Medical Disease and Differential Diagnosis

A.1. How is the diagnosis of lung carcinoma made? What is your prediction for the most likely type of malignancy?

The initial presenting symptoms in patients with lung cancer may be respiratory, but in the majority of cases, they are constitutional and nonspecific, mainly related to metastatic disease. Nonproductive cough, dyspnea, hemoptysis, and chest pain, along with an unresolved lung infiltrate on chest radiography should suggest carcinoma. The diagnosis and extent of the disease are confirmed by sputum cytology, bronchoscopy and endobronchial brush biopsy, biopsy of palpable lymph nodes in the neck or axilla, needle aspiration biopsy, mediastinoscopy, and possibly exploratory thoracoscopy or thoracotomy. Before any major surgical approach, an extensive evaluation is done to diagnose metastases that would contraindicate surgery.

Cancers of the lung account for 16% of all malignancies and nearly 30% of cancer deaths worldwide. Bronchogenic carcinomas represent the vast majority of lung cancers in patients requiring surgical resection and can be classified into four major types: small cell, large cell, squamous cell, and adenocarcinoma. For surgical purposes, lung tumors are classified as non–small cell or small cell. The former are amenable to surgical resection, while the latter tend to be nonresectable and are treated medically.

Further subclassification of lung tumors involves the TNM system, in which T designates tumor site, size, and local extent; N, the presence and location of regional lymph node involvement; and M, the presence of distal metastases beyond the ipsilateral hemithorax. The TNM classification is used in the staging of bronchogenic carcinomas and helps predict response to therapy. In general, small cell carcinomas that spread beyond possible resection by the time of presentation are primarily managed with chemotherapy, with or without radiation. The 5-year survival after chemotherapy and radiation with curative intent is approximately 20%. In contrast, non–small cell cancers found to be localized at the time of presentation should be considered for

primary resection. The 5-year survival depends on tumor staging, but can be as high as 85% for small tumors without regional lymph node involvement or metastases (stage I). Approximately 45% of patients present with circumscribed extrapulmonary disease or lymphatic spread to the ipsilateral mediastinal or subcarinal lymph nodes (stage IIIa). Their 5-year postresection survival is less than 20%.

Fauci AS, Braunwald E, Kasper DL, et al., eds. *Harrison's Principles of Internal Medicine*. 17th ed. New York: Graw-Hill; 2008:551–562.

Shibutani HC. Pulmonary resection. In: Youngberg JA, Lake CL, Wilson RS, eds. *Cardiac, Vascular and Thoracic Anesthesia*. New York: Churchill Livingstone; 2000:639–659.

Spiro SG, Gould MK, Colice GL. Initial evaluation of patients with lung cancer: symptoms, signs, laboratory tests, and paraneoplastic syndromes: ACCP evidence-based clinical practice guidelines (2nd ed.). *Chest*. 2007;132:149S–160S.

A.2. What are the less common manifestations of bronchogenic carcinoma?

Other manifestations of lung tumors are primarily related to mass effects or altered metabolism. In addition to bronchial obstruction (evident in this patient) that can lead to postobstructive pneumonia, mass effects include invasion into the chest wall and pleura, compression of great vessels (e.g., superior vena cava syndrome) and heart, tracheobronchial displacement, paresis of the recurrent laryngeal or phrenic nerves as well as the sympathetic chain, and Pancoast syndrome (pain and upper extremity weakness secondary to invasion of the brachial plexus as well as the first and second thoracic and eighth cervical nerve roots). Recognized metabolic manifestations of small cell lung tumors include symptoms that resemble those of Cushing syndrome (from ectopic adrenocorticotropic hormone production), carcinoid syndrome, hypercalcemia and hypophosphatemia (resulting from ectopic parathyroid hormone or parathyroid hormone-related peptide), hypokalemia (caused by ectopic adrenocorticotropic hormone secretion), and hyponatremia (from inappropriate secretion of antidiuretic hormone and possibly atrial natriuretic factor). Neurologic paraneoplastic syndromes include Eaton-Lambert myasthenic syndrome, peripheral neuritis involving both motor and sensory components, cerebellar degeneration, retinopathy, limbic encephalopathy, and autonomic neuropathy. An autoimmune process has been suggested for these findings, and it seems to be more common in patients with limited disease.

Extrathoracic spread of the tumor can contribute to the nonspecific presentation. Structures involved include the bones, liver, adrenal glands, intra-abdominal and subcutaneous lymph nodes, brain, and spinal cord.

Fauci AS, Braunwald E, Kasper DL, et al., eds. *Harrison's Principles of Internal Medicine*. 17th ed. New York: McGraw-Hill; 2008:554.

Slinger PD, Johnston MR. Preoperative assessment for pulmonary resection. *J Cardiothorac Vasc Anesth*. 2000;14:202–211.

Spiro SG, Gould MK, Colice GL. Initial evaluation of patients with lung cancer: symptoms, signs, laboratory tests, and paraneoplastic syndromes: ACCP evidence-based clinical practice guidelines (2nd ed.). *Chest*. 2007;132:149S–160S.

A.3. The patient has a long history of cigarette smoking. What is the significance of this finding?

Cigarette smoking promotes the development of chronic obstructive pulmonary disease (COPD), which includes chronic bronchitis and emphysema, and is strongly associated with an increased incidence of stroke, myocardial infarction, and cancer

(lung, oral cavity, larynx, and esophagus) compared to nonsmokers. Evidence of chronic pulmonary changes can be seen in the preoperative pulmonary function tests. Pulmonary hypertension and cor pulmonale may also occur in this patient population.

In patients who smoke at the time of surgery, there is an increased risk of postoperative complications and a higher 5-year mortality rate. Respiratory failure, pneumonia, aspiration, air leak, and atelectasis are all increased. Therefore, smoking cessation is highly recommended at the time of diagnosis. Although carboxyhemoglobin concentrations decline substantially within 12 hours of smoking cessation, it remains unclear for how long smoking must be discontinued to see a significant reduction in postthoracotomy complications. For patients undergoing cardiac surgery, a period of 2 months is suggested to see an impact on postoperative pulmonary function. This is mainly due to improved mucociliary function. In patients undergoing thoracic surgery, the benefits of smoking cessation must be balanced with the risk of local tumor growth and metastatic spread, which may preclude resectability. Four weeks has been suggested as an acceptable time by several studies in this population.

Colice GL, Shafazand S, Griffin JP, et al. Physiologic evaluation of the patient with lung cancer being considered for resectional surgery: ACCP evidence-based clinical practice guidelines (2nd ed.). *Chest*. 2007;132:161S–177S.

Erhunmwunsee L, Onaitis MW. Smoking cessation and the success of lung cancer surgery. *Curr Oncol Rep*. 2009;11:269–274.

Licker MJ, Widikker I, Robert J, et al. Operative mortality and respiratory complications after lung resection for cancer: impact of chronic obstructive pulmonary disease and time trends. *Ann Thorac Surg*. 2006;81:1830–1837.

Mason DP, Subramanian S, Nowicki ER, et al. Impact of smoking cessation before resection of lung cancer: a society of thoracic surgeons general thoracic database study. *Ann Thorac Surg*. 2009;88:362–371.

Pedoto A, Heerdt PM. Postoperative care after pulmonary resection: postanesthesia care versus intensive care unit. *Curr Opin Anaesthesiol*. 2009;22:50–55.

B. Preoperative Evaluation and Preparation

B.1. How would you evaluate the patient preoperatively?

Preoperative evaluation should include a complete history, physical examination, and laboratory tests (e.g., complete blood count, basic metabolic profile, coagulation study, electrocardiogram, chest radiography, and computed tomographic imaging). The main goal for preoperative evaluation is to identify in advance those patients at risk for major postoperative complications and optimize their functional status. A positive smoking history, especially if current, cough, sputum production, orthopnea, and dyspnea are hallmarks of cardiopulmonary disease and should be further investigated. An abnormal exercise tolerance, such as the inability to climb at least three flights of stairs or walk for 6 minutes, may indicate a patient with compromised response to the stress of anesthesia and surgery. The majority of patients are now admitted to the hospital on the day of surgery; therefore, a brief review of symptoms, physical limitations, interval changes, and airway anatomy should be performed before entering the operating room.

In addition to routine preoperative testing, patients scheduled for lung resection usually undergo pulmonary function testing to help define the relative risks of the planned resection. Respiratory function can be assessed by:

- **Respiratory mechanics:** Forced vital capacity (FVC), forced expiratory volume in the first second (FEV_1), and the ratio between residual volume and total lung capacity (RV/TLC).

- **Cardiopulmonary reserve:** Maximal oxygen uptake (VO_2 max), stair climbing, 6-minute walk, and shuttle walk. VO_2 max in particular is the gold standard for aerobic capacity and cardiorespiratory fitness. Patients with VO_2 max value less than 10 mL/kg/min are at increased risk for postoperative morbidity and mortality.
- **Lung parenchymal function:** Diffusing lung capacity for carbon monoxide (DLCO), partial pressure of oxygen in arterial blood (Pao_2), and partial pressure of arterial carbon dioxide ($Paco_2$). Predicted postoperative DLCO and FEV_1 less than 40% to 44% are significant independent predictors for increased postoperative morbidity and mortality.

Colice GL, Shafazand S, Griffin JP, et al. Physiologic evaluation of the patient with lung cancer being considered for resectional surgery: ACCP evidence-based clinical practice guidelines (2nd ed.). *Chest*. 2007;132:161S–177S.

Datta D, Lahiri B. Preoperative evaluation of patients undergoing lung resection surgery. *Chest*. 2003;123:2096–2103.

Pedoto A, Heerdt PM. Postoperative care after pulmonary resection: postanesthesia care versus intensive care unit. *Curr Opin Anaesthesiol*. 2009;22:50–55.

Slinger PD, Johnston MR. Preoperative assessment for pulmonary resection. *J Cardiothorac Vasc Anesth*. 2000;14:202–211.

Van Tilburg PM, Stan H, Hoogsteden HC, et al. Pre-operative pulmonary evaluation of lung cancer patients: a review of the literature. *Eur Resp J*. 2009;33:1206–1215.

B.2. What are the pulmonary function guidelines that indicate an increased risk for morbidity and mortality?

The reported mortality from lung resection is between 2% and 4%, mainly as a result of pneumonia, respiratory failure, bronchopleural fistula, empyema, and pulmonary embolism. Respiratory insufficiency occurs in approximately 5% of patients following lung resection and is associated with a 50% mortality rate. Advanced age and the associated increased incidence of concomitant nonpulmonary disease seem to contribute to this outcome. An increased risk of postoperative complications can be predicted by the following:

- **Spirometry:** Spirometric parameters, such as FEV_1/FVC ratio and FEV_1 (reflective of the degree of airway obstruction), as well as static volumes (such as inspiratory and total lung capacity), are used to define the severity of COPD. Several studies have indicated a strong correlation between predicted postoperative FEV_1 and DLCO and a respective increase in morbidity and mortality, especially for open procedures and extensive dissection. Concerning values are summarized in Table 2.1.
- **Arterial blood gases:** Historically, hypercapnia ($Paco_2$ greater than 45 mm Hg) was considered an exclusion criterion for lung resection. However, no independent correlation has been found with an increased mortality. Patients who are hypercapnic often have a low predicted postoperative FEV_1 and an abnormal exercise capacity, which preclude surgery. Preoperative hypoxemia (Pao_2 less than 50 mm Hg, and percentage of available hemoglobin saturated with oxygen [Sao_2] less than 90%) has been associated with an increased risk of postoperative complications. However, baseline hypoxemia can be the result of ventilatory mismatch caused by obstructive tumors that once resected may theoretically improve gas exchange.

Other factors influencing outcome include patient comorbidities and functional status, the extent and location of the proposed surgical resection, and whether the patient has undergone preoperative induction chemotherapy. An improvement in both surgical and anesthesia techniques has broadened the criteria for surgical respectability. As evident from lung volume reduction studies, patients with severely impaired pulmonary function (e.g. FEV_1 less than 1 L) can still undergo surgical resection under general anesthesia without prohibitive risk for postoperative complications. Moreover,

Table 2.1 Minimal Pulmonary Function Test Criteria for Various-Sized Pulmonary Resections

TEST	UNIT	NORMAL	PNEUMONECTOMY	LOBECTOMY	BIOPSY OR SEGMENTAL
MBC	L/min	>100	>50	>40	>25
MBC	Percentage predicted	100%	>50%	>40%	>25%
FEV_1	Liters	>4	>2.1–1.7	>1.2–1.0	>0.6–0.9
FEV_1	Percentage	>80% FVC	>50% FVC	>40% FVC	>40% FVC
$FEV_{25\%–75\%}$	Liters	>2	>1.6	>0.6–1.6	>0.6

$FEV_{25\%–75\%}$, forced expiratory volume from 25% to 75% of forced vital capacity; FEV_1, forced expiratory volume in first second; MBC, maximum breathing capacity.

the development of minimally invasive surgical techniques has raised the question of whether standard selection criteria should always be adopted.

Although preoperative pulmonary function tests are valid indices of physiologic performance, the actual predictive utility of a range of values for a single parameter is poorly defined. Overall, emphasis has been directed toward integrating multiple aspects of the preoperative evaluation (e.g., respirometry, ventilation-perfusion scanning, extent of planned resection, patient functional status) into the estimate of postoperative function. Better postoperative analgesia techniques, early ambulation, and thromboprophylaxis have all contributed to improve outcomes after major lung resection in patients at high risk.

Boffa DJ, Allen MS, Grab JD, et al. Data from The Society of Thoracic Surgeons General Thoracic Surgery database: the surgical management of primary lung tumors. *J Thorac Cardiovasc Surg*. 2008;135:247–254.

Hartigan PM, Pedoto A. Anesthetic considerations for lung volume reduction surgery and lung transplantation. *Thorac Surg Clin*. 2005;15:143–157.

Matsubara Y, Takeda S, Mashimo T. Risk stratification for lung cancer surgery: impact of induction therapy and extended resection. *Chest*. 2005;128:3519–3525.

Pedoto A, Heerdt PM. Postoperative care after pulmonary resection: postanesthesia care versus intensive care unit. *Curr Opin Anaesthesiol*. 2009;22:50–55.

Slinger PD, Campos J. Anesthesia for thoracic procedures. In: Miller RD, ed. *Miller's Anesthesia*. 9th ed. New York: Churchill Livingstone; 2010:1820–1826.

C. Intraoperative Management

C.1. How would you premedicate, monitor, and anesthetize this patient?

Current practice in most institutions dictates that patients arrive at the hospital the day of surgery; thus, traditional oral or parenteral premedication before transport to the operating room is largely obsolete. Bronchoscopy and mediastinoscopy are generally ambulatory procedures, necessitating a relatively rapid hospital discharge. Because thoracoscopy in this patient is only a possibility, intravenous midazolam immediately on entry into the operating room would seem appropriate for anxiolysis and subsequent amnesia. In addition, a small intravenous dose (0.2 mg) of glycopyrrolate can be considered as an antisialagogue, particularly in patients who smoke.

However, the potential for tachycardia should be considered, especially in patients with coronary artery disease or atrial fibrillation.

During mediastinoscopy, intermittent compression or occlusion of the innominate artery can occur. Therefore, the blood pressure cuff should be placed on the left arm and the pulse oximeter on the right hand. In the case of innominate artery compression, a damping of the pulse oximetry trace will be evident and blood pressure measurements will remain accurate. Although rare, injury to vascular structures can occur, potentially necessitating sternotomy. Patient positioning and placement of electrocardiography leads should be considered accordingly. Arterial access is not routinely used for this procedure unless the patient has clinical indications for continuous hemodynamic monitoring. In this case, the catheter should be placed in the left radial artery as well. Body temperature should be monitored and a warming blanket applied. Despite the potential for a short procedure, elderly patients in particular can become hypothermic. Induction, maintenance of anesthesia, and muscle relaxation can be achieved with relatively short-acting agents. Propofol is usually used for induction of general anesthesia followed by rocuronium, vecuronium, or cisatracurium to facilitate tracheal intubation via a single-lumen endotracheal tube (ETT). Anesthesia can be maintained with a potent inhalational agent in oxygen or air, if oxygen saturation tolerates it, and 2 to 3 μg per kg of fentanyl often provides sufficient analgesia for the procedure. Local anesthetic can be infiltrated in the wound by the surgeon at the beginning or at the end of the procedure. Nonsteroidal anti-inflammatory drugs (NSAIDs) are used by some providers as adjuvant agents; nevertheless, the potential for bleeding in a closed space in ambulatory patients should be considered. Finally, many clinicians choose to avoid the use of nitrous oxide because of the potential for the mediastinoscope to enter the pleural space and create a pneumothorax.

Ehrenwerth J, Brull SJ. Anesthesia for thoracic diagnostic procedures. In: Kaplan JA, Slinger PD, eds. *Thoracic Anesthesia*. 3rd ed. Philadelphia: Churchill Livingstone; 2003:174–195.

Molins L, Fibla JJ, Perez J, et al. Outpatient thoracic surgical programme in 300 patients: clinical results and economic impact. *Eur J Cardiothorac Surg*. 2006;29:271–275.

Wilson RS. Anesthesia for bronchoscopy and mediastinoscopy. In: Youngberg JA, Lake CL, Wilson RS, eds. *Cardiac, Vascular and Thoracic Anesthesia*. New York: Churchill Livingstone; 2000:660–669.

C.2. How many types of bronchoscopes are available and what are the intraoperative considerations of each one?

Three types of bronchoscopes are currently in use: flexible fiber-optic, rigid ventilating, and rigid Venturi.

The flexible fiber-optic bronchoscope can be used either in sedated patients under local anesthesia (allowing examination of vocal cords movements) or under general anesthesia with a laryngeal mask airway or an ETT. For the awake or sedated examination, viscous lidocaine can be gargled to anesthetize the upper airway and a 2% or 4% lidocaine solution inhaled via nebulizer mask to reach the lower airway. Bilateral superior laryngeal nerve blocks or transtracheal block can be added. Intravenous sedation can be achieved with 0.5-mg increments of midazolam, 10 μg of remifentanil boluses or propofol infusion. Alternatively, dexmedetomidine (as a bolus of 0.5 to 1 μg per kilogram over 10 minutes followed by a continuous infusion of 0.2 to 0.7 μg/skg/hr) can also be used, its main advantage consisting of amnesia without impaired ventilation. If the oropharynx is adequately anesthetized, a laryngeal mask airway can be inserted without discomfort in sedated patients and used to assist ventilation and provide higher Fio_2 concentrations.

In contrast, rigid bronchoscopy usually necessitates general anesthesia. Although spontaneous ventilation has been used, the risk of tracheal trauma is high with coughing. If not contraindicated, muscle relaxation is usually used. The rigid ventilating

bronchoscope has a side-port adapter that can be attached to the anesthesia machine, allowing the delivery of a high flow rate. A variable air leak usually exists around the bronchoscope, so high flow rates of inspired gases or packing of the oropharynx are needed. Significant loss of volatile anesthetic into the operating room environment needs to be considered; thus, the use of total intravenous technique is a good alternative.

The rigid Venturi-effect bronchoscope relies on an intermittent high flow (20 to 60 L per minute), high pressure (50 lbs per square inch [psi]) oxygen jet to entrain air and insufflate the lungs. The jet is delivered through a reducing valve (25 psi) into a 16- or 18-gauge needle inside and roughly parallel to the lumen of the bronchoscope. Major disadvantages of this bronchoscope are the lack of control of the inspired oxygen concentration and the inability to administer inhaled anesthetics. Accordingly, anesthesia must be maintained by intravenous techniques. Inadequate ventilation (with resultant hypercapnia) can also occur.

Rigid bronchoscopic procedures can be relatively short; therefore, continuous succinylcholine infusion still remains an option for these procedures. If not contraindicated, small doses of nondepolarizing muscle relaxants can also be used. When followed by another procedure (such as the mediastinoscopy scheduled for this patient), an intermediate-duration nondepolarizing muscle relaxant is often desirable.

Ehrenwerth J, Brull SJ. Anesthesia for thoracic diagnostic procedures. In: Kaplan JA, Slinger PD, eds. *Thoracic Anesthesia*. 3rd ed. Philadelphia: Churchill Livingstone; 2003:174–195.

Wilson RS. Anesthesia for bronchoscopy and mediastinoscopy. In: Youngberg JA, Lake CL, Wilson RS, eds. *Cardiac, Vascular and Thoracic Anesthesia*. New York: Churchill Livingstone; 2000:660–669.

C.3. What are the indications for cervical mediastinoscopy? Are there potential complications?

Cervical mediastinoscopy is usually performed to establish a diagnosis for specific lesions within the mediastinum or as a staging procedure for malignancy to determine mediastinal lymph nodes spread. If lymph nodes are positive for malignancy by frozen section, the patient is probably not a surgical candidate and the planned lung resection aborted.

Conventional cervical mediastinoscopy involves a small incision at the sternal notch for the insertion of the mediastinoscope and sampling of lymph nodes. The pleural space is generally not entered intentionally, and, therefore, a chest tube is not indicated. Occult pneumothorax can occur as a complication, so a chest radiograph is usually obtained before discharge. Complications during mediastinoscopy are relatively rare (1% to 2%) and generally result from trauma to adjacent structures (pleura, trachea, esophagus, superior vena cava, azygos vein, innominate artery, pulmonary artery, and aorta) or nerve injury (recurrent laryngeal or phrenic nerve). Should a major vascular structure be perforated, blood loss can be rapid and profound, necessitating emergent sternotomy. Because packing or vascular clamps may be applied to the superior vena cava, clinicians should always have a plan for establishing venous access in the lower extremity.

Ehrenwerth J, Brull SJ. Anesthesia for thoracic diagnostic procedures. In: Kaplan JA, Slinger PD, eds. *Thoracic Anesthesia*. 3rd ed. Philadelphia: Churchill Livingstone; 2003:174–195.

Wilson RS. Anesthesia for bronchoscopy and mediastinoscopy. In: Youngberg JA, Lake CL, Wilson RS, eds. *Cardiac, Vascular and Thoracic Anesthesia*. New York: Churchill Livingstone; 2000:660–669.

C.4. The decision was made to proceed with a right VATS middle lobectomy. How would this alter your management?

Although not uniformly regarded as necessary for lung resection, an arterial catheter will be placed in the left (dependent) radial artery. Lung isolation can be achieved via bronchial blocker placed inside or outside the existing ETT or with a left-sided double-lumen tube. Although a right middle lobectomy per se is not an absolute indication for lung isolation, the thoracoscopic approach dictates complete lung collapse to achieve surgical exposure. Because of the side of surgery and the variable take-off of the right upper lobe bronchus, the best choice for lung isolation would be a left double-lumen tube.

Single-lung ventilation is associated with certain disadvantages and complications. The most notable is the large and variable alveolar-to-arterial oxygen tension difference ($P[A\text{-}a]O_2$) that occurs as a result of continued perfusion to the nondependent, nonventilated lung. However, the incidence of severe hypoxemia and hypercarbia is relatively small and often the result of double-lumen tube malposition resulting from overinflation of the endobronchial cuff, surgical manipulation of the bronchus, or head extension or flexion during positioning. Other complications include traumatic laryngitis and tracheobronchial rupture resulting from bronchial cuff overinflation, forceful placement, or airway pathology.

Brodsky JB, Fitzmaurice B. Modern anesthetic techniques for thoracic operations. *World J Surg.* 2001;25:162–166.

Campos JA. Lung separation techniques. In: Kaplan JA, Slinger PD, eds. *Thoracic Anesthesia.* 3rd ed. Philadelphia: Churchill Livingstone; 2003:159–173.

Shibutani HC. Pulmonary resection. In: Youngberg JA, Lake CL, Wilson RS, eds. *Cardiac, Vascular and Thoracic Anesthesia.* New York: Churchill Livingstone; 2000:639–659.

C.5. What are the indications for single-lung ventilation and how can it be accomplished?

Absolute and relative indications for lung separation are listed in Table 2.2. Several techniques can be used to provide single-lung ventilation, including double-lumen tubes, bronchial blocking catheters passed outside or inside the ETT, ETTs with incorporated bronchial blocking catheters (Univent ETT), or conventional ETTs placed endobronchially. Currently, DLTs remain the most common method for achieving lung isolation. Although DLTs of variable design and material have been used in the past (e.g., Robertshaw, Carlens, and White), the models most commonly used today are disposable and made of polyvinylchloride. Such a tube was the chosen for this procedure. DLTs are available in five sizes: 28, 35, 37, 39, and 41 French (size in French = 3.14 times external diameter in millimeters or 4 times the internal diameter + 2), and two sides (right and left). Although the general rule is that average-sized men usually accommodate a no. 39 F and average-sized women a no. 37 F, there is no clear correlation between age, height, weight, and DLT size. Accordingly, some clinicians advocate the use of small DLTs in all patients. A variety of techniques have been described based on measurements of airway size derived from radiographic or computed tomographic imaging, but these have been questioned across gender and ethnicity. A properly sized double-lumen tube should pass atraumatically through the glottis, advance easily into the trachea and bronchus, and exhibit an air leak when the bronchial cuff is deflated.

Several types of bronchial blockers are available (see section C.9). Disadvantages of blockers include the fact that lung collapse can be slow, especially in patients with severe COPD, and catheter tips can be dislodged during surgical manipulation of the hilum or stapled in the bronchial stump. Bronchial blocking catheters remain a good

Table 2.2 Indications for Single-Lung Ventilation

ABSOLUTE	
1. To isolate from spillage or contamination	• Infection: Bronchiectasis and lung abscess • Massive hemorrhage
2. To control the distribution of ventilation	• Bronchopleural fistula • Bronchopleural cutaneous fistula • Giant unilateral lung cyst or bulla • Tracheobronchial tree disruption or trauma • Surgical procedures on major conducting airway (i.e., pneumonectomy or sleeve resection) • Life-threatening hypoxemia resulting from unilateral lung disease • Unilateral bronchopulmonary lavage (pulmonary alveolar proteinosis)
3. To facilitate surgical exposure	• Video- and robotic-assisted thoracoscopic surgery
RELATIVE	
1. Facilitation of surgical exposure—high priority	• Thoracic aortic aneurysm • Pneumonectomy • Upper lobectomy • Mediastinal exposure • Pulmonary resection via median sternotomy
2. Facilitation of surgical exposure—low priority	• Esophageal resection • Middle and lower lobectomies and segmental resection • Procedures on the thoracic spine
3. Severe hypoxemia resulting from unilateral lung disease	

option for lung isolation in patients who have difficult airways or when postoperative mechanical ventilation is needed. Patients with a fresh tracheostomy are also good candidates for the use of blockers.

Campos JA. Lung separation techniques. In: Kaplan JA, Slinger PD, eds. *Thoracic Anesthesia*. 3rd ed. Philadelphia: Churchill Livingstone; 2003:159–173.

Slinger PD, Campos J. Anesthesia for thoracic procedures. In: Miller RD, ed. *Miller's Anesthesia*. 9th ed. New York: Churchill Livingstone; 2010:1833–1841.

C.6. What are the contraindications to the use of double-lumen endotracheal tubes (DLTs)?

Placement of a DLT should be carefully considered in the following situations:

- Patients whose upper airway anatomy may preclude safe insertion of the tube (recessed jaw, prominent teeth, bull neck, anterior larynx, mandibular surgery, and neck radiation).
- Patients with lesions present somewhere along the pathway of the tube that could be traumatized, such as airway stricture or endoluminal tumors.
- Small patients for whom a no. 35 F tube is too large to fit comfortably through the larynx and a no. 28 F tube is considered too small.

- Critically ill patients who have a single-lumen tube already in place and who cannot tolerate cessation of mechanical ventilation and positive end-expiratory pressure (PEEP) for a short time.

Under these circumstances, single-lung ventilation can be achieved via an endobronchial blocker or an ETT placed into a mainstem bronchus. However, using a single-lumen tube in the mainstem bronchus for lung isolation can be suboptimal. Distal airway trauma may occur, and the cuff can bulge at the carina, causing significant airway compression and potential mucosal ischemia. When placed on the right side, the right upper lobe can also be occluded by the cuff of the tube, preventing the ability to ventilate.

Brodsky JB, Fitzmaurice B. Modern anesthetic techniques for thoracic operations. *World J Surg*. 2001;25:162–166.

Campos JA. Lung separation techniques. In: Kaplan JA, Slinger PD, eds. *Thoracic Anesthesia*. 3rd ed. Philadelphia: Churchill Livingstone; 2003:159–173.

Slinger PD, Campos J. Anesthesia for thoracic procedures. In: Miller RD, ed. *Miller's Anesthesia*. 9th ed. New York: Churchill Livingstone; 2010:1833–1841.

C.7. Would you use a right-sided or left-sided double-lumen tube?

A left-sided DLT is generally preferable for most procedures because the variable origin of the right upper lobe (1.5 to 2.0 cm below carina) may complicate maintaining good placement of a right-sided tube. Nevertheless, in an institution in which the use of right-sided DLT is routine, the incidence of hypoxemia, hypercarbia, or high airway pressures was found to be the same for patients managed with left or right DLTs. The left mainstem bronchus is much longer than the right (approximately 5.0 to 5.5 cm versus 1.5 to 2.0 cm), thus providing a greater margin for error in positioning. A right-sided DLT is indicated in the case of pathology of the left mainstem bronchus, such as large exophytic lesions, tight bronchial stenosis, tracheobronchial disruption, endobronchial stent, and distortion by an adjacent tumor or a thoracoabdominal aneurysm. Other indications include left pneumonectomy or lung transplantation so that the surgical field is not encumbered by a foreign body that could be included in the staple line or prevent suturing of the donor lung. At the end of a pneumonectomy, the stump can be protected from positive pressure ventilation by leaving the tracheal side clamped until the patient returns to spontaneous ventilation; for a left lung transplant, the right lung continues being ventilated during the reconstruction phase. Right double-sided lumens are contraindicated in the case of anomalous take-off of the right upper bronchus above the tracheal carina, commonly referred to as a "pig bronchus."

Campos JA. Lung separation techniques. In: Kaplan JA, Slinger PD, eds. *Thoracic Anesthesia*. 3rd ed. Philadelphia: Churchill Livingstone; 2003:159–173.

Ehrenfeld JM, Walsh JL, Sandberg WS. Right- and left-sided Mallinckrodt double-lumen tubes have identical clinical performance. *Anesth Analg*. 2008;106:1847–1852.

Slinger PD, Campos J. Anesthesia for thoracic procedures. In: Miller RD, ed. *Miller's Anesthesia*. 9th ed. New York: Churchill Livingstone; 2010:1833–1841.

C.8. How do you know that the tube is in the correct position?

The position of a double-sided lumen may be confirmed by listening to breath sounds of each lung while clamping each lumen. In patients with emphysema, breath sounds may be decreased or diffuse, making auscultation difficult and unreliable. Thus, fiber-optic bronchoscopy is often helpful in confirming position before placing

the patient in the lateral decubitus position. During bronchoscopy, the tracheal cartilaginous rings are anterior and the tracheal membrane is posterior. Therefore, right versus left can be discerned by the relationship of the mainstem bronchi to the anterior cartilaginous rings and the posterior membrane (Fig. 2.1A). In addition, the right upper lobe take-off (which usually arises from the lateral aspect of the right mainstem bronchus, just below the tracheal carina) is a useful landmark when the airway anatomy has been obscured by bleeding, edema, or radiation-induced changes or has been distorted by extrinsic compression. Left DLT position and depth are confirmed by inserting the fiber-optic bronchoscope in the tracheal lumen. The entire right mainstem bronchus should be visible and the tracheal lumen orifice of the DLT should be 1 to 2 cm above the tracheal carina. When properly positioned, the upper part of the blue endobronchial cuff is visualized just below the tracheal carina in the left mainstem bronchus (Fig. 2.1B). If a right DLT is used, correct positioning is confirmed by visualization of the bronchial cuff in the right mainstem bronchus (Fig. 2.1C) and visualization of the right upper lobe orifice through a slot on the

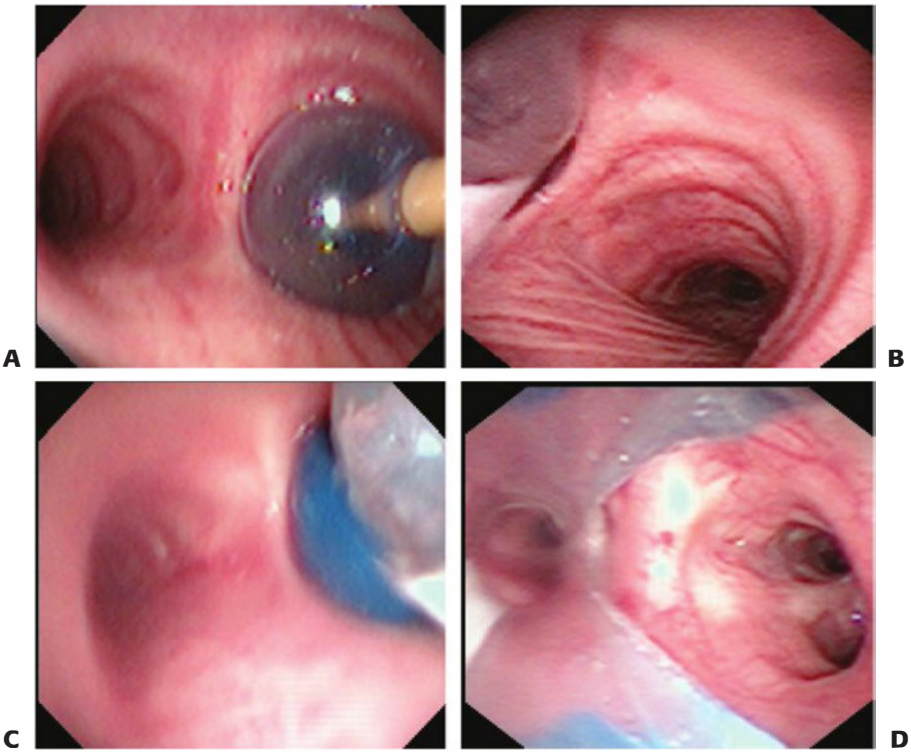

Figure 2.1 Representative bronchoscopic images of a bronchial blocker and DLT placement. **A.** Normal tracheal anatomy with cartilaginous rings anteriorly and membranous trachea posteriorly; this helps define left versus right. A bronchial blocking catheter is seen in the right mainstem bronchus. **B.** Placement of a left-sided DLT; the upper portion of the endobronchial cuff is evident as well as the orifice of the right upper lobe just below tracheal carina. **C.** Placement of a right-sided DLT; the upper portion of the endobronchial cuff is evident in the right mainstem bronchus. **D.** The orifice of the right upper lobe visualized through the slot on the lateral aspect of the bronchial side of a right-sided DLT.

lateral surface of the DLT (Fig. 2.1D). For both left-sided and right-sided tubes, the bronchoscope should also be inserted in the bronchial lumen to evaluate the distance between the tip of the tube and the distal bifurcation of the bronchus. Double lumen tube position should be reconfirmed after the patient is positioned laterally, before inflating the blue cuff and isolating the lung.

Campos JA. Lung separation techniques. In: Kaplan JA, Slinger P, eds. *Thoracic Anesthesia*. 3rd ed. Philadelphia: Churchill Livingstone; 2003:159–173.

C.9. How many types of bronchial blockers are available? What are the advantages and disadvantages of bronchial blockers?

Several blockers are available, leaving ample choice to the operator and the institution to develop a preference. Advantages and disadvantages of blockers are listed in Table 2.3.

- **Fogarty embolectomy catheters** can be used to isolate the lung, although not specifically made for this purpose. Number 7 French (7F) Fogarty catheters come with either a 12- or 20-mL high-pressure, low-volume balloon in both latex and nonlatex models. They have a metallic stylet that can be bent to facilitate endobronchial placement. In the case of dislodgment, the stylet can be reinserted and the blocker repositioned. Fogarty catheters have no communicating central channel; therefore, continuous positive airway pressure (CPAP) or suction cannot be applied intraoperatively. Ventilation should be discontinued and the ventilation circuit depressurized as long as the patient tolerates it before filling the balloon. Lung collapse then occurs by absorption of oxygen. The catheters are usually placed outside a single-lumen ETT and positioned via fiber-optic bronchoscopy (Fig. 2.1A). If placed inside the ETT, a connector such as a two-swivel adaptor is needed to facilitate insertion of both the catheter and a bronchoscope.
- **Arndt blockers** (wire-guided endobronchial blocker) are available in no. 5F, 7F, and 9F with elliptical or spherical cuffs (low pressure, high volume), the latter particularly advantageous to isolate the right lung. They are usually inserted through the ETT via a three-way connector (catheter, bronchoscope, ventilation circuit). Their positioning is facilitated by an inner wire that has a loop at the distal tip. The flexible bronchoscope is placed through the loop to facilitate positioning. The wire is then removed once the blocker is in position, leaving an inner lumen that allows for suctioning or CPAP. Once the wire loop has been removed, it can be reinserted, allowing repositioning of the blocker in case it dislodges.

Table 2.3 Advantages and Disadvantages of Bronchial Blockers

ADVANTAGES	DISADVANTAGES
• Able to use in adults and children too small to fit a double-lumen tube	• Unable to suction efficiently
• Difficult airway	• Need to be positioned via fiber-optic bronchoscopy
• If double-lumen tube contraindicated	• Difficult for right mainstem position and RUL isolation, when the take-off is too close to the carina.
• Placed inside the ETT	• Tracheal occlusion if proximal dislodgment.
• No need to change ETT in the case of postoperative mechanical ventilation	• Cross ventilation if the cuff is not completely inflated.
	• Possible stapling in the stump if not retracted at the appropriate time

ETT, endotracheal tube; RUL, right upper lobe.

- **Cohen blockers** are similar in shape to the Arndt blockers, but they use a positioning "wheel" to facilitate placement. By turning the wheel, the distal portion of the blocker deflects. The main advantage of this blocker is its placement in the left mainstem because of its steep angle. Disadvantages of the Cohen blocker include cost and the fact that the wheel is very delicate. They also come in only one size (no. 9F).
- **Univent tubes** consist of an ETT with a built-in silicon bronchial blocking catheter. The main advantage is the fact that the ETT may be left in place in case the patient requires postoperative mechanical ventilation. The main disadvantage is the bulkiness of the device. The outer diameter ranges from 9.7 to 13.7 mm (for a 6.0 to 8.0 inner diameter tube), with the potential to cause subglottic edema and stenosis in case of long-term use. The inner diameter is quite narrow, making suctioning or fiber-optic bronchoscopy difficult. The silicon blocker in the Univent is now available as an isolated item (**Fuji blocker**) that comes with a double stylet that has a preformed bend at the tip. It has a spherical cuff (ideally more suited to isolate the right mainstem bronchus) and three different sizes (no. 5F, 7F, and 9F).

Arndt GA, DeLessio ST, Kranner PW, et al. One-lung ventilation when intubation is difficult: presentation of a new endobronchial blocker. *Acta Anaesthesiol Scand.* 1999;43:356–358.

Campos JH. An update on bronchial blockers during lung separation techniques in adults. *Anesth Analg.* 2003;97:1266–1274.

Slinger PD, Campos J. Anesthesia for thoracic procedures. In: Miller RD, ed. *Miller's Anesthesia*. 9th ed. New York: Churchill Livingstone; 2010:1833–1841.

C.10. How will systemic oxygenation be monitored during single-lung ventilation? What is the mechanism of pulse oximetry?

Pulse oximetry has become the hallmark for monitoring arterial oxygenation during lung resection, decreasing the need for repeated measurements of arterial blood gases. This technique uses spectrophotoelectric oximetric principles to determine oxygen saturation. Pulse oximeters are multiple-wavelength plethysmographs. The amplitude of the pulse is a function of arterial distention, hemoglobin oxygen saturation of the arterial blood inflow, and light wavelength. Hemoglobin saturation in arterial blood is the result of the ratio between the pulse amplitude of red (660 nm = deoxyhemoglobin) and infrared (940 nm = oxyhemoglobin) light. Pulsatile waveform is a characteristic of arterial blood flow, so there is no interference from surrounding venous blood, skin, connective tissue, or bone. Arterial pulsations cause changes in light absorption, which are used to calculate oxygen saturation. Adequate finger pulsation generally is lost with hypothermia of a few degrees, hypotension (mean blood pressure less than 50 mm Hg), and infusion of vasoconstrictive drugs. Dyshemoglobinemias (such as carboxyhemoglobin, methemoglobin, and sulfhemoglobin), as well as intravenous dye injection, can also affect its accuracy.

Other methods to continuously monitor arterial oxygenation include transcutaneous oxygen tension ($Ptco_2$) and arterial oxygen tension using an indwelling electrode. $Ptco_2$ requires special site preparation, airtight probe mantling, and a potentially harmful local source of heat to induce arterialization. Moreover, $Ptco_2$ fails to perfectly reflect true arterial oxygenation. An indwelling arterial oxygen electrode is inserted into the arterial line and may increase the incidence of thromboembolism.

Brodsky JB, Fitzmaurice B. Modern anesthetic techniques for thoracic operations. *World J Surg.* 2001;25:162–166.

Tremper KK, Barker SJ. Pulse oximetry. *Anesthesiology.* 1989;70:98–108.

C.11. The patient was placed in the lateral decubitus position. Describe the effects of lateral positioning on pulmonary blood flow and respiration.

In both upright and supine positions, the right lung receives approximately 55% of the total blood flow and the left lung receives the remaining 45%. In the lateral decubitus position, gravity causes a vertical gradient in blood flow distribution. Therefore, perfusion of the dependent lung is significantly greater than the nondependent counterpart. When the right lung is nondependent, it receives 45% of the total blood flow while 55% perfuses the dependent left lung. When the left lung is nondependent, it receives 35% of the total blood flow, while right lung receives 65%. Therefore, the average blood flow of the nondependent lung is approximately 40% of the total blood flow with the dependent lung being perfused with the remaining 60% (Fig. 2.2).

Respiratory Effects

The lateral decubitus position causes mechanical interference with chest wall movement, decreasing lung expansion. The dependent chest wall is constricted by the operating room table, and lateral movements are limited by the bolsters or the "bean-bag" used to hold the patient in position. Moreover, there is an increase in intra-abdominal pressure with general anesthesia and muscle relaxation, with a decrease in diaphragmatic movements. Mismatching of ventilation and perfusion in the lateral position is the result of gravity, with redistribution of blood flow toward the dependent lung and compression of the dependent lung by the mediastinum and the abdominal contents. In awake, spontaneously breathing subjects, the lower (dependent) diaphragm is still able to contract more efficiently, maintaining ventilation to the dependent lung and matching the increased perfusion. In contrast, when the patient is anesthetized, with or without paralysis, most of the ventilation is preferentially switched to the more compliant upper lung. Perfusion increases in the lower lung, resulting in an increased degree of ventilation-perfusion mismatch.

Rehder K, Hatch DJ, Sessler AD, et al. The function of each lung of anesthetized and paralyzed man during mechanical ventilation. *Anesthesiology.* 1972;37:16.

Shibutani HC. Pulmonary resection. In: Youngberg JA, Lake CL, Wilson RS, eds. *Cardiac, Vascular and Thoracic Anesthesia.* New York: Churchill Livingstone; 2000:639–659.

Walff KE, Aulin I. The regional lung function in the lateral decubitus position during anesthesia and operations. *Acta Anesthesiol Scand.* 1972;16:195–205.

C.12. What is hypoxic pulmonary vasoconstriction (HPV)?

HPV is an autoregulatory mechanism to prevent ventilation-perfusion mismatch and improve arterial oxygenation. The precise mechanism for HPV is still not completely

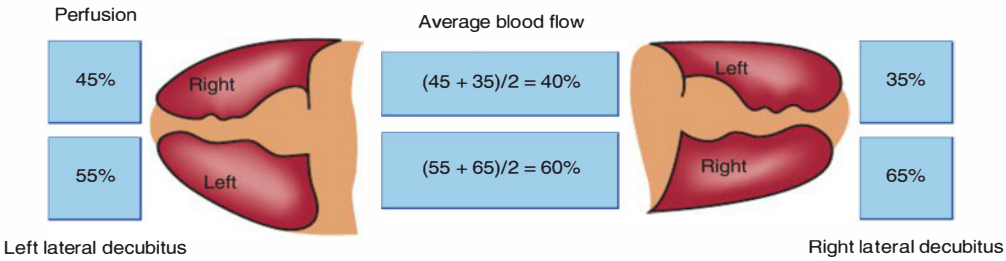

Figure 2.2 Changes in blood perfusion with the lateral decubitus position.

understood. Hypotheses include an increase in pulmonary arterial smooth muscle reactive oxygen species and activation of redox-based oxygen sensors, as well as an increase in intracellular calcium by activation of multiple pathways. HPV is triggered by a decrease in Pa_{O_2} within the lung from low F_IO_2, hypoventilation, or atelectasis. The selective increase of vascular resistance in the hypoxic parenchyma diverts blood away to the better ventilated normoxic lung, decreasing the amount of shunt flow.

Increasing evidence indicates that significant systemic oxidative stress can be elicited by hyperoxic reperfusion of a lung in which HPV has been sustained for an extended period because of the collapse produced by single-lung ventilation. Although the exact ramifications of this insult remain to be clarified, clinical data suggest an association between the magnitude of the oxidative stress and postoperative cardiopulmonary complications.

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Connolly MJ, Aaronson PI. Cell redox state and hypoxic pulmonary vasoconstriction: recent evidence and possible mechanisms. *Respir Physiol Neurobiol*. 2010;174:165–174.

Misthos P, Katsaragakis S, Milingos N, et al. Postresectional pulmonary oxidative stress in lung cancer patients: the role of one-lung ventilation. *Eur J Cardiothorac Surg*. 2005;27:379–382.

Nagendran J, Stewart K, Hoskinson M, et al. An anesthesiologist's guide to hypoxic pulmonary vasoconstriction: implications for managing single-lung anesthesia and atelectasis. *Curr Opin Anaesthesiol*. 2006;19:34–43.

C.13. What are the effects of anesthetic agents on HPV and their clinical implications?

Several clinical studies have failed to demonstrate a decrease in HPV during single-lung ventilation and total intravenous anesthesia. Intravenous anesthetics, such as thiopental, ketamine, morphine, and fentanyl, have no direct effect on HPV, whereas propofol seems to enhance it. In contrast, inhalational anesthetics have been shown to inhibit HPV in a dose-related fashion but usually at concentrations much higher than used clinically. Other nonanesthetic drugs such as β-agonists and antagonists, calcium channel blockers, nitrovasodilators, and theophylline may influence the effects of inhalation anesthetics on shunting and arterial oxygenation during single-lung ventilation.

- The end result of an increased shunt on Pa_{O_2} depends on the absolute level of the initial shunt and the inspired oxygen concentration used. In clinical practice, nearly 100% oxygen is often used during single-lung ventilation. Even when shunt is increased, Pa_{O_2} usually remains well above 100 mm Hg and oxygen saturation and oxygen content hardly change.
- Inhalational agents inhibit HPV, but they also decrease cardiac output and oxygen consumption and may cause a decrease in mixed venous-oxygen tension. If cardiac output decreases more than oxygen consumption, there will be a decrease in Pv_{O_2}, which is a potent stimulus for HPV. A low cardiac output will result in a decreased perfusion of the collapsed lung (where there is an increase in pulmonary vascular resistance as a result of HPV). Nevertheless, the presence of chronic, irreversible vascular disease in the nondependent lung may impair HPV response.
- The presence of disease in the dependent lung will decrease the ability of accepting blood flow redistribution, thereby decreasing the HPV effect of the nondependent lung.
- Direct surgical manipulation may cause the release of vasoactive substances, such as thromboxane and prostacyclins, promoting local vasodilatation and blunting HPV, with a subsequent increase in shunt.

Boldt J, Müller M, Uphus D, et al. Cardiorespiratory changes in patients undergoing pulmonary resection using different anesthetic management techniques. *J Cardiothorac Vasc Anesth.* 1996;10:854–859.

Brodski J. Management of hypoxia during one lung ventilation. Anesthesia, Pain, Intensive Care and Emergency. APICE 2007: Nov 9–11. Chapter 27, pages 291–298.

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C.14. Discuss pulmonary blood flow distribution, shunt flow, and Pao_2 (F_Io_2 = 1.0) during single-lung ventilation in the lateral position.

When the nondependent lung is collapsed, HPV will increase pulmonary vascular resistance and decrease lung blood flow in this area. If no complicating factors exist, HPV should decrease blood flow to that lung by approximately 50%, causing a total reduction from 40% to 20% of the total. The resulting nondependent/dependent lung blood flow ratio during single-lung ventilation should be 20%:80%.

Once atelectatic, all the blood flowing into the nonventilated lung is shunt flow. Therefore, single-lung ventilation creates an obligatory right-to-left transpulmonary shunt that was not present during double-lung ventilation. If no shunt existed during double-lung ventilation (ignoring the normal 1% to 3% physiologic amount from the bronchial, pleural, and thebesian circulation), an ideal total shunt flow of 20% would be expected during single-lung ventilation. Pao_2 with a fractional inspired O_2 concentration (F_Io_2) equal to 1 should be approximately 280 mm Hg if hemodynamic and metabolic states are normal. Clinically, Pao_2 (F_Io_2 = 1) ranges from 150 to 250 mm Hg.

Marshall BE, Marshall C. Continuity of response to hypoxic pulmonary vasoconstriction. *J Appl Physiol.* 1980;59:189–196.

Shibutani HC. Pulmonary resection. In: Youngberg JA, Lake CL, Wilson RS, eds. *Cardiac, Vascular and Thoracic Anesth*esia. New York: Churchill Livingstone; 2000:639–659.

C.15. How could you improve oxygenation during single-lung ventilation?

When hypoxia occurs during single-lung ventilation, the goal is to optimize the match between ventilation and perfusion on the dependent lung or increase the amount of oxygen in the shunted blood of the collapsed lung.

Ventilated lung

a. Optimize ventilation

- Use 100% oxygen
- Check the position of the double-lumen tube with a fiber-optic bronchoscope
- Ventilate manually to determine whether higher or lower tidal volumes or inspiratory pressures are beneficial.
- Set minute ventilation to maintain $Paco_2$ at 40 mm Hg (hypocapnia may inhibit HPV in the nondependent lung, whereas hyperventilation may increase airway pressure and promote blood flow to the nonventilated lung).
- Apply 5 cm H_2O of PEEP. It may be beneficial if larger tidal volumes delivered manually improved arterial saturation (i.e., recruitable alveoli). Alternatively, if tidal volumes are too large, adding PEEP may overdistend alveoli that are already open and compress blood vessels, diverting blood to the nonventilated lung and worsening the shunt.
- Use two-lung ventilation intermittently.

b. Increase perfusion:
- Selective vasodilators (inhaled nitric oxide, inhaled prostacyclin PGI_2)

Collapsed lung:

a. Oxygenate shunt blood: A variety of approaches have been described but must be carefully considered for VATS procedures because most involve some degree of lung reexpansion and therefore may affect surgical visualization.
- Insufflate oxygen continuously: A flow of about 3 L per minute allowed to freely circulate will often increase arterial oxygen saturation 3% to 4%.
- Intermittent single breath with oxygen.
- Partially reexpand the nonventilated lung then keep the lumen side closed.
- Apply continuous CPAP.
- Differential CPAP to the collapsed lung and PEEP to the ventilated lung has been described, but is rarely necessary and generally impractical for VATS procedures.
- High-frequency ventilation to the nonventilated lung.

b. Decrease the shunt
- Use drugs to augment HPV (phenylephrine, norepinephrine, almitrine).
- Clamp lobar vessels or the pulmonary artery of the nonventilated lung temporarily (rarely necessary).

Brodsky J. Anesthesia, Pain, Intensive Care and Emergency. APICE 2007: Nov 9–11. Chapter 27, pages 291–298.

Slinger PD, Campos J. Anesthesia for thoracic procedures. In: Miller RD, ed. *Miller's Anesthesia*. 9th ed. New York: Churchill Livingstone; 2010:1851–1853.

C.16. A right middle lobectomy was performed. Would you extubate the trachea at the end of the procedure?

After routine lung resection, the trachea can be extubated as long as the patient meets all criteria and has adequate analgesia. If the patient cannot maintain adequate oxygenation and ventilation, postoperative mechanical support is indicated. Under most circumstances, when patients require postoperative ventilatory support, it is advantageous to change the double-lumen tube to a single-lumen ETT. Double-lumen tubes have a large outer diameter, which can cause airway edema and trauma if left in place for prolonged time. They are likely to move with patient movement, and it is difficult to suction through them. Spontaneous ventilation avoids the potential hazards of positive pressure on the suture lines of the new bronchial stump or parenchymal air leaks. The combination of modest CPAP and pressure support ventilation is usually preferable to controlled intermittent mandatory ventilation.

Higgins TL. Post thoracotomy complications. In: Kaplan JA, Slinger PD, ed. *Thoracic Anesthesia*. 3rd ed. Philadelphia: Churchill Livingstone; 2003:159–173.

D. Postoperative Management

D.1. What are the immediate life-threatening complications that follow lobectomy or pneumonectomy?

Serious complications after lobectomy include lobar collapse, massive hemorrhage caused by loosening of pulmonary vessels ligatures, bronchopleural fistula from disruption of a bronchial stump, and pulmonary torsion and infarction resulting from increased mobility of a lobe. Mediastinal shift, pleural effusion, hemothorax, chylothorax, empyema, and pulmonary edema can also occur.

Pneumonectomy can be complicated by supraventricular arrhythmias, acute respiratory insufficiency, nerve injuries (phrenic, vagus, or recurrent laryngeal) during radical hilar dissection or excision of mediastinal tumors, cardiac herniation (in the case of intrapericardial approach), acute right heart failure, and right-to-left shunting across a patent foramen ovale as a result of increased pulmonary vascular resistance and increased right ventricular pressure.

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D.2. Why is it important to control postoperative pain? How would you achieve this?

Adequate postoperative analgesia is important not only for patient comfort, but also to minimize pulmonary complications, allowing the patient to breathe deeply, cough effectively, and ambulate. Several options are available, depending on the institution and surgical preferences.

Epidural and Intrathecal Analgesia

A trend has been shown toward a decrease in morbidity and mortality after lung resection since the introduction of regional analgesia. Thoracic or lumbar epidural analgesia may be achieved by a single injection or a continuous infusion of local anesthetic alone or in combination with an opiate. In order to reduce the volume required to produce an effect and lessen the chance of hypotension and motor weakness, the catheter can be placed as close as possible to the dermatomes to be covered. A low concentration of local anesthetic such as 0.1% or 0.05% bupivacaine combined with an opiate (e.g., fentanyl 5 to 10 μg per mL, hydromorphone 8 μg per mL or sufentanyl 0.1 μg per mL) produces synergistic effects that can reduce the sympathetic blockade that may occur with a more concentrated local anesthetic alone. In addition, the presence of local anesthetics seems to increase the affinity of the narcotic for the opioid receptors. The use of thoracic epidural analgesia with local anesthetic plus opiate has been shown to improve postoperative pulmonary function. Potential complications of thoracic epidural technique can be related to the placement (inadvertent dural puncture, trauma to the spinal cord, hematoma) or drug administration (intravascular injection of local anesthetics with resultant cardiovascular and central nervous system toxicity). In addition, clinicians should carefully consider the patient's use of long acting antiplatelet medications.

Intrathecal injection of opiates has been successfully used preoperatively or intraoperatively to provide postoperative pain relief for 18 to 24 hours. In comparison to epidural injection, intrathecal opiates (in particular morphine) are associated with an increased incidence of late respiratory depression (4% to 7% compared to less than 1% for epidural administration). The advantages of neuraxial techniques compared to systemic opiates include selective blockade of spinal pain receptors with minimal sympathetic blockade, no loss of motor function, and greater predictability of pain relief. Epidural opiates in combination with local anesthetics block the presynaptic and postsynaptic neuron cells of the substantia gelatinosa of the spinal cord by passive diffusion across the dura into the cerebrospinal fluid. The lipophilic narcotics, such as fentanyl 0.1 mg, methadone 5 mg, and meperidine 30 to 100 mg, have a relatively short onset of action (less than 12 minutes). They provide significant pain relief in 20 to 30 minutes, which can last for 6 to 7 hours. In contrast, a hydrophilic opiate, such as morphine, in a 5-mg dose, has a relatively slow onset of action of (15 to 30) minutes; provides maximal pain relief in 40 to 60 minutes; and has a duration of action of more than 12 hours. The most serious complications of epidural narcotics are early and late

respiratory depression. Other side effects include urinary retention, pruritus, nausea, and vomiting. The narcotic antagonist naloxone can reverse all the aforementioned side effects but will also reverse the analgesia, so it must be used cautiously. Overall, unlike epidural local anesthetic, epidural opioids have not been shown to decrease the incidence of postoperative respiratory complications.

Systemic Opioids and Nonsteroidal Anti-inflammatory Drugs

Systemic administration of opiates is often used alone or in combination with other modalities to control postoperative pain. Patient-controlled analgesia, often in combination with NSAIDs, can be used in the postoperative period. When used as a single modality, systemic opioids require plasma concentrations that are usually associated with sedation, potential respiratory depression, hypoventilation, cough inhibition, and reduced sighing. Even when used as patient-controlled analgesia, pain control is often suboptimal because of fluctuations in the drug plasma concentration. NSAIDs such as ketorolac, diclofenac, ketoprofen, and indomethacin can be used as adjuvants to parenteral opiates, particularly for the treatment of shoulder pain associated with chest tube placement. Potential side effects for NSAIDs include gastric bleeding, platelet dysfunction, and renal insufficiency in patients who are severely fluid restricted, especially the elderly.

Low-dose intravenous ketamine infusion (0.2 μg/kg/hr) has been used as an adjuvant in the postoperative period, especially in patients with chronic pain. Psychomimetic side effects are a possibility, but are rare at this dosage. Intravenous dexmedetomidine 0.2 to 0.5 μg/kg/hr is another alternative in the postoperative period. Its central α_2-agonism potentiates analgesia, allowing a decrease in the dose of intravenous narcotics. Hypotension and bradycardia are potential side effects.

Intercostal and Paravertebral Nerve Block

Intercostal and paravertebral nerve blocks with long-acting local anesthetics can be used to control pain after thoracoscopy or thoracotomy. In both cases, if single injections are used, they have a short duration (6 to 8 hours when bupivacaine is used). Therefore, catheters can be left in place and dosed postoperatively. Intercostal blocks can be done under direct vision by the surgeon before closing the chest cavity or percutaneously before awakening the patient. The intercostal nerves to be blocked are at the level of the incision and two or three interspaces above and below. Of the three main sensory divisions of the intercostal nerve (posterior, lateral, and anterior cutaneous nerve), the posterior branch cannot be blocked with this approach, limiting its usefulness in the case of a posterolateral incision. The quality of analgesia with this technique alone is inferior to the one achieved via the epidural route. Intercostal catheters are indicated as part of a multimodality treatment when neuroaxial blocks are contraindicated (e.g., patients on anticoagulation or tumor involvement of the epidural space) or for minimally invasive procedures. Because the rate of systemic absorption of the local anesthetic from the intercostal space is quite high, there is an increased risk of systemic toxicity.

Paravertebral blocks and catheters can be used preoperatively or postoperatively, and used in combination with parenteral opiates and NSAIDs, used as an alternative to thoracic epidural analgesia. In order to be effective, multiple levels need to be blocked. The failure rate for this technique is relatively high (6% to 10%) and can be decreased by locating the space via ultrasound guidance or under direct vision by the surgeon before closing the chest. Pneumothorax (especially if bilateral blocks are attempted), hypotension, local anesthetic toxicity because of the high vascularity of the area, and inadvertent total spinal are all potential risks. Advantages compared with epidural analgesia include less hypotension, less nausea or vomiting, and the ability to block just the surgical side.

Intrapleural Regional Analgesia

Intrapleural analgesia utilizes the percutaneous introduction of a catheter between the parietal and visceral pleura for the injection of local anesthetic. Analgesia is

thought to occur as a result of (1) diffusion of local anesthetic through the parietal pleura and the innermost intercostal muscle to the intercostal nerves (where the block occurs), (2) block of the intrathoracic sympathetic chain, and (3) direct action of local anesthetic on nerve endings within the pleura. Nevertheless, the quality of analgesia is extremely variable and unfavorable compared to that of other modalities. The local anesthetic can be lost through the thoracotomy drainage, it can be diluted by extravasated blood and tissue fluid in the pleural space, or it can be sequestered and channeled because of the decreased movements of the operated lung. Moreover, in the sitting position, the local anesthetic pools in the costophrenic angle, limiting the quality of analgesia. The use of multiple or fenestrated catheters may achieve a more even distribution over the pleura and improve the quality of analgesia. However, this technique is rarely used today.

Cryoanalgesia

Long-lasting (3 to 4 weeks up to 6 months) intercostal nerve block can be obtained by cryoablation. Two 30- to 60-second freeze cycles (−60° C), separated by a 5-second thaw period, are applied to each of the nerves selected. Although cryoanalgesia was initially shown to effectively relieve pain and improve postoperative pulmonary function, more detailed studies have revealed a significant incidence of paresthesia and postthoracotomy pain syndrome.

Transcutaneous Electrical Nerve Stimulation

Transcutaneous electrical nerve stimulation (TENS) relies on the application of brief pulses of current via electrodes to the affected area. The advantages of TENS include low cost, ease of application, and lack of undesirable side effects. Nevertheless, TENS has a weak analgesic effect. It is generally reserved for adjunctive use with narcotics to relieve mild to moderate postthoracotomy pain. It is ineffective if the pain is severe and is contraindicated in patients with pacemakers, defibrillators, and infusion pumps, because the current could produce interference.

Shoulder Pain after Lung Resection

Independently from the analgesia technique used and the surgical approach, approximately 80% of patients who have undergone lung resection complain of ipsilateral shoulder pain that is unresponsive to epidural block or systemic opioid. Possible causes for shoulder pain include referred pain from diaphragmatic irritation, chest tube placement (too far at the apex of the hemithorax), the posterior end of a large posterolateral incision, or surgical positioning in patients with arthritis. Shoulder pain usually responds to anti-inflammatory agents, and often resolves on the second postoperative day. Phrenic nerve infiltration and brachial plexus block have been used, but have the potential of causing diaphragmatic dysfunction.

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CHAPTER 3

Aspiration Pneumonitis and Acute Respiratory Failure

Manuel L. Fontes, Sean Garvin, and Fun-Sun F. Yao

A 20-YEAR-OLD FULL-TERM PREGNANT WOMAN was rushed to the operating room for emergency cesarean section because of fetal distress. During emergence from general anesthesia, the patient vomited and aspirated.

A. Management of Aspiration

1. Delineate the risk factors for aspiration pneumonitis.
2. What is Mendelson syndrome?
3. What is the critical pH value and volume of aspirate to cause Mendelson syndrome?
4. How does aspiration pneumonitis differ from aspiration pneumonia?
5. You suspect the patient has aspirated; what is your initial management strategy?
6. Would you give prophylactic antibiotics?
7. Would you give steroid therapy?
8. Would you irrigate the bronchial tree with bicarbonate or saline solution?
9. How would you prevent aspiration during emergency surgery?

B. Acute Lung Injury

The patient was extubated in the recovery room. Chest x-ray films showed questionable mottled density in the posterior segments of the right upper lobe. Six hours after being transferred to the floor, she was found to be dyspneic and cyanotic. On auscultation of the chest, significant wheezing was noted, and the results of the most recent analysis of arterial blood gases showed the following: pH, 7.26; $Paco_2$, 55 mm Hg; Pao_2, 55 mm Hg; and HCO_3^-, 20 mEq per L on room air.

1. Define acute lung injury (ALI) and acute respiratory distress syndrome (ARDS).
2. What are the common causes of ARDS?
3. Describe the pathogenesis of ALI.

4. What are the radiographic findings in ARDS?
5. Describe protective-ventilation strategy in ALI and ARDS.
6. Define pulmonary compliance.

C. Mechanical Ventilation

The patient did not improve after receiving 50% oxygen through a face mask. A second arterial blood gas analysis showed the following: pH, 7.25; $Paco_2$, 50 mm Hg; Pao_2, 55 mm Hg; and CO_2 content, 22 mEq per L. The respiratory rate was 40 breaths per minute.

1. Interpret the blood gases.
2. What is your clinical plan?
3. What are the criteria for mechanical ventilation?
4. Describe the basic modes of mechanical ventilation. Discuss the advantages and disadvantages of pressure-controlled and volume-controlled modes.
5. What control mode would you select for this patient?
6. What initial ventilator settings will you prescribe for this patient (tidal volume, respiratory frequency, inspiratory oxygen fraction, etc.)?
7. Describe the potential hemodynamic effects of positive pressure ventilation (PPV).
8. What are the adverse effects of mechanical ventilation?

D. Therapeutic Approaches for Ventilatory Support

After intubation and mechanical ventilation, the oxygenation did not improve. On Fio_2, 0.7, the arterial blood gas analysis showed the following: pH, 7.30; $Paco_2$, 40 mm Hg; Pao_2, 57 mm Hg; and CO_2 content, 18 mEq per L.

1. What factors determine oxygen delivery?
2. How will you treat the hypoxemia?
3. What are the major factors governing oxygen toxicity?
4. What is the mechanism of oxygen toxicity?
5. What are your criteria to start positive end-expiratory pressure (PEEP)?
6. How does PEEP improve arterial oxygenation?
7. How would you determine the best PEEP and the optimal PEEP?
8. What are the cardiovascular effects of PEEP?
9. What is pressure-support ventilation (PSV)? Discuss its advantages.
10. Describe the rationale for prone-position ventilation and its effect on oxygenation.
11. How is liquid ventilation accomplished?
12. What are the indications and contraindications for extracorporeal membrane oxygenation (ECMO)? How many ways can it be used? What are its results?
13. What is high-frequency positive pressure ventilation (HFPPV)? What are its characteristics?
14. What are the frequencies used in high-frequency ventilation (HFV)? How are they classified?
15. What are the indications and precautions for HFV?
16. What is nitric oxide (NO)? What is the role of inhaled NO in the treatment of ARDS?

E. Weaning from Ventilatory Support

The patient's condition improved after respiratory support with 12 cm H_2O PEEP. Arterial blood gas analysis showed the following: pH, 7.45; $Paco_2$, 35 mm Hg; Pao_2, 150 mm Hg; and Fio_2, 0.75.

1. What would you do now?
2. The patient continued to improve. When would you consider weaning the patient from the respirator? Discuss the criteria for weaning.
3. Describe weaning by synchronized intermittent mandatory ventilation (SIMV), pressure support, continuous positive airway pressure (CPAP), and T-piece.

A. Management of Aspiration

A.1. Delineate the risk factors for aspiration pneumonitis.

Aspiration pneumonitis arises most often from aspiration of gastric content that is both acidic and voluminous. It can also occur from aspiration of oropharyngeal content. Several patient characteristics lead to the development of aspiration. These include:

- Neurologic dysphagia
- Disruption of gastroesophageal junction
- Anatomic abnormalities of the upper aerodigestive tract
- General anesthesia
- Poor oral hygiene
- Pharmacologic agents that alter consciousness (e.g., sedatives, antipsychotics, antidepressants, narcotics)
- Extremes of age (elderly, neonates)

The risk of aspiration pneumonitis is approximately 10% in patients presenting to the hospital after a drug overdose. This condition used to be very common in general anesthesia and accounted for most obstetric morbidity and mortality. The most recent report suggests an incidence of 1 in 3,000 patients receiving general anesthetics; however, the mortality remains very high and accounts for 10% to 30% of all deaths related to anesthesia. The elderly, particularly the nursing home population, is at increased risk of aspiration secondary to both an increased incidence of pharyngeal dysmotility and gastroesophageal reflux. Aspiration pneumonia and pneumonitis are the most common causes of death in patients with dysphagia caused by neurologic disorders, a condition that affects approximately 300,000 to 600,000 people yearly in the United States.

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A.2. What is Mendelson syndrome?

Mendelson first described acute chemical aspiration pneumonitis in 1946. The triphasic sequence beginning with immediate respiratory distress, bronchospasm, cyanosis, tachycardia, and dyspnea, following with partial recovery, and concluding with a final phase of gradual respiratory recovery is characteristic of Mendelson syndrome. No signs of mediastinal shift are seen, but chest x-ray films usually show irregular mottled densities. This syndrome is due to the irritation of bronchioles by gastric hydrochloric acid, producing bronchiolar spasm, a peribronchiolar exudates, and congestion.

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A.3. What is the critical pH value and volume of aspirate to cause Mendelson syndrome?

The critical pH value is 2.5. At a pH value higher than 2.5, the response is similar to that of distilled water. Maximal pulmonary damage is achieved at an aspirate pH value of 1.5. A patient is thought to be at risk when there is more than 25 mL (0.4 mL per kg) of gastric contents and the pH value of the gastric contents is less than 2.5. However, the risk of hypercapnia, acidosis, and subsequent pneumonitis may be increased if particulate matter is in the aspirate.

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A.4. How does aspiration pneumonitis differ from aspiration pneumonia?

Aspiration pneumonitis generally is attributed to a chemical injury of the lungs from aspiration of gastric content (Fig. 3.1). The more acidic the pH value and the more voluminous the gastric content, the more severe the chemical burn. Food particles, independent of the acidity, also can cause a chemical injury. Aspiration pneumonitis consists of two phases: The first stage peaks within the first few hours after the aspiration and is mostly related to the caustic effect of the low pH value of the aspirate on the cells lining the alveolar-capillary interface; the second phase generally peaks at approximately 6 hours and is characterized both by infiltration of neutrophils into the alveoli and the lung interstitium and by an inflammatory process identical to that observed in other types of ALI.

Aspiration pneumonia differs from aspiration pneumonitis. It is caused by bacterial pathogens. The chemical irritation and inflammation resulting from aspiration pneumonitis may predispose an individual to developing an aspiration pneumonia. As such, the incidence of aspiration pneumonia in the population at risk (see section A.1) is much greater because a small amount of either oropharyngeal or gastric content that is colonized with bacteria is sufficient to cause injury, particularly in the elderly and the immunocompromised host. In the community, most commonly the causative organisms are indigenous oral flora. These are predominantly anaerobes (e.g., *Bacteroides* species, *Fusobacterium* species, *Peptostreptococcus* species) and streptococci. Both *Haemophilus influenzae* and *Streptococcus pneumoniae* first colonize the oropharynx and access the tracheobronchial tree and alveoli after aspiration to cause community-acquired pneumonia. In nosocomial bacterial pneumonia (i.e., aspiration in the hospital), in addition to the usual oral flora pathogens, *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella* species, *Enterobacter* species, and *Pseudomonas* species may be involved. Ventilator-associated

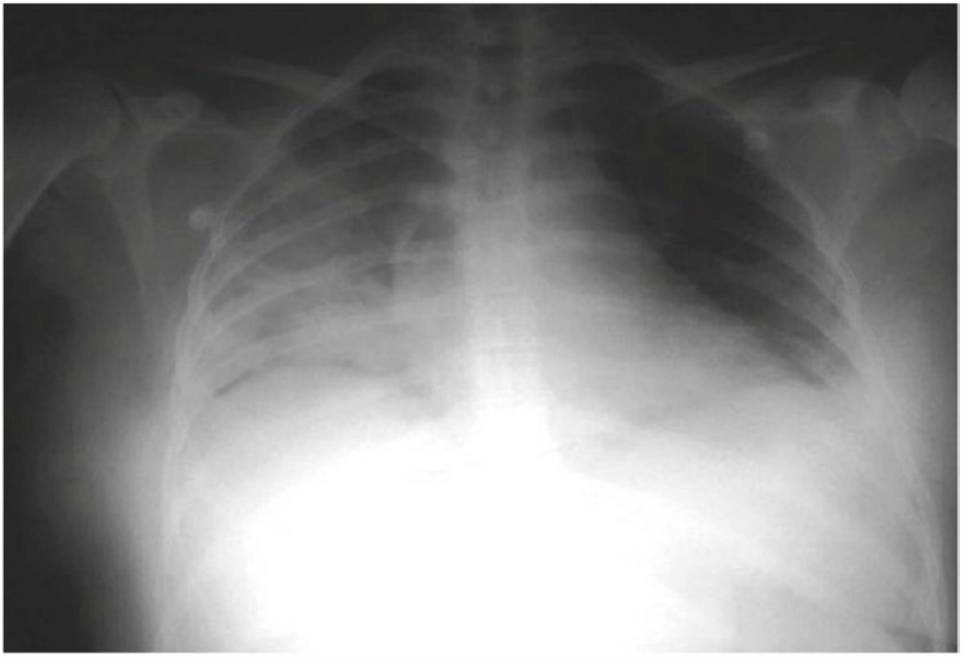

Figure 3.1 Typical radiographic findings in aspiration pneumonitis.

pneumonia may require broader antibiotic coverage. The term *aspiration pneumonia* is used specifically to describe radiographic evidence of infiltrate in a patient who is at risk of oropharyngeal aspiration. More than 50% of adults aspirate some amount of oropharyngeal secretion during sleep; however, very little sequelae arise from this for several reasons: First, the burden of virulent bacteria in "normal" pharyngeal secretions is low; second, the host is able to clear the aspirate through ciliary transport and cough reflexes; and third, the status of the immune system is noncompromised.

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Robbins J, Gensler G, Hind J, et al. Comparison of 2 interventions for liquid aspiration on pneumonia incidence: a randomized trial. *Ann Intern Med*. 2008;148:509.

Smith Hammond C. Cough and aspiration of food and liquids due to oral pharyngeal dysphagia. *Lung*. 2008;186(suppl 1):S35.

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van Westerloo DJ, Knapp S, et al. Aspiration pneumonitis primes the host for an exaggerated inflammatory response during pneumonia. *Crit Care Med*. 2005;33:1770–1778.

A.5. You suspect the patient has aspirated; what is your initial management strategy?

Rapidly tilt the operating table to a 30-degree head-down position to have the larynx at a higher level than the pharynx and to allow gastric content to drain to the outside. While an assistant maintains cricoid pressure, suction the mouth and pharynx as rapidly as possible. Next, endotracheal intubation should be performed (if the patient had been extubated) with immediate inflation of the endotracheal cuff to prevent further aspiration. Quickly suction through the endotracheal tube before administering 100% oxygen by PPV. This is to prevent pushing aspirated material beyond your reach. Suction should be brief to avoid cardiac arrest from hypoxia.

An orogastric tube should be inserted to empty the stomach. The pH value of the gastric content should be determined.

Tracheobronchial aspirate is collected for culture and sensitivity tests. Auscultation of the chest will determine whether diminished breathing sounds, wheezing, rales, and rhonchi are present. If bronchospasm is noted, β_2-agonists such as albuterol or terbutaline may be administered through metered-dose inhaler adapters to the anesthetic circuit.

The earliest and most reliable sign of aspiration is hypoxemia, which follows aspiration of even the mildest and most benign aspirate. Therefore, analysis of arterial blood gases should be performed to determine the severity of hypoxemia. Early application of PEEP is recommended to improve pulmonary function.

Abouleish E, Grenvik A. Vomiting, regurgitation, and aspiration in obstetrics. *Pa Med*. 1974;77:45–58.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1222.

d'Escrivan T, Guery B. Prevention and treatment of aspiration pneumonia in intensive care units. *Treat Respir Med.* 2005;4(5):317–324.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease.* 5th ed. Philadelphia: Churchill Livingstone; 2008:559.

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A.6. Would you give prophylactic antibiotics?

The initial aspirate, excluding feculent aspirate, is usually sterile and remains so for the first 24 hours. Thereafter, the aspiration pneumonitis can become aspiration pneumonia either from contamination of the initial aspirate or secondarily from aspiration of a colonized oropharyngeal secretion in a host that now has tracheobronchial and alveolar damage. Colonization cultures may demonstrate gram-positive or gram-negative superinfection or both, usually with *Escherichia, Klebsiella, Staphylococcus, Pseudomonas,* and *Bacteroides* or with anaerobes. Prophylactic antibiotic has *not* been shown to improve mortality or reduce secondary infection rates. Cultures must be taken as soon as possible after aspiration and thereafter as clinically indicated. The antibiotic therapy is given according to the sensitivity test result. Prophylactic use of broad-spectrum antibiotics may lead to drug-resistant bacterial and fungal superinfection. However, if intestinal obstruction is a possibility, antimicrobial therapy for the possibility of anaerobic and gram-negative infection may be warranted. Although data supporting the use of prophylactic antibiotics are lacking, it is not unusual for clinicians to prescribe such therapy in settings in which the host is considered immunocompromised (e.g., elderly and critically ill patients). If one or several antibiotics have been administered, prompt withdrawal should occur with laboratory or clinical evidence of no infection. In contrast, the use of antibiotics in aspiration pneumonia is unequivocally indicated (e.g., third-generation cephalosporins, fluoroquinolones, or piperacillin).

Allewelt M, Schuler P, Bolcskei PL, et al. Ampicillin + sulbactam vs clindamycin +/− cephalosporin for the treatment of aspiration pneumonia and primary lung abscess. *Clin Microbiol Infect.* 2004;10(2):163–170.

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Miller RD, ed. *Miller's Anesthesia.* 7th ed. Philadelphia: Churchill Livingstone Elsevier; 2010:2879–2897.

Ott SR, Allewelt M, Lorenz J, et al. Moxifloxacin vs ampicillin/sulbactam in aspiration pneumonia and primary lung abscess. *Infection.* 2008;36:23.

Rebuck JA, Rasmussen JR, Olsen KM. Clinical aspiration-related practice patterns in the intensive care unit: a physician survey. *Crit Care Med.* 2001;29(12):2239–2244.

Snydman DR, Jacobus NV, McDermott LA, et al. Lessons learned from the anaerobe survey: historical perspective and review of the most recent data (2005–2007). *Clin Infect Dis.* 2010;50(suppl 1):S26.

Wu YC, Hsu PK, Su KC, et al. Bile acid aspiration in suspected ventilator-associated pneumonia. *Chest.* 2009;136:118.

A.7. Would you give steroid therapy?

The value of systemic corticosteroids is controversial. The rationale for immediate use of corticosterowwwids is to reduce inflammation and stabilize lysosomal membranes. In addition, they have been shown to prevent pulmonary cellular damage

by protecting type II alveolar pneumocytes and to attenuate agglutination of leukocytes and platelets.

In experimental studies, the effectiveness of corticosteroid therapy appeared to be related to the pH value of aspirates. When the pH value of the aspirate was in the narrow range of 1.5 to 2.5, corticosteroid therapy was beneficial in treating acid-aspiration pneumonitis. Dexamethasone, given 0.08 mg per kg every 6 hours, decreased pulmonary water content significantly starting at 24 hours, with return to the normal range by 72 hours. When the pH value of the aspirate was less than 1.5, the pulmonary parenchymal damage was maximal. Therefore, the steroid therapy was not effective. When the pH value of the aspirate was higher than 2.5, the response was similar to that of water.

Wolfe, Bone, and Ruth found that pneumonia caused by gram-negative bacteria was more frequent after aspiration in patients treated with corticosteroids than in those who were not. Similarly, studies in animals have failed to demonstrate a beneficial effect of corticosteroids on pulmonary function, lung injury, alveolar-capillary permeability, or outcome after acid aspiration. Furthermore, because of the failure of two multicenter, randomized, controlled trials to demonstrate a benefit of high-dose corticosteroids in patients with ARDS, the administration of corticosteroids cannot be recommended.

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Bernard GR, Luce JM, Sprung CL, et al. High-dose corticosteroids in patients with the adult respiratory distress syndrome. *N Engl J Med*. 1987;317:1565–1570.

Downs JB, Chapman RL Jr, Modell JH, et al. An evaluation of steroid therapy in aspiration pneumonitis. *Anesthesiology*. 1974;40:129–135.

Dudley WR, Marshall BE. Steroid treatment for acid-aspiration pneumonitis. *Anesthesiology*. 1974;40:136–141.

Lee M, Sukumaran M, Berger HW, et al. Influence of corticosteroid treatment on pulmonary function after recovery from aspiration of gastric contents. *Mt Sinai J Med*. 1980;47:341–346.

Lowrey LD, Anderson M, Calhoun J, et al. Failure of corticosteroid therapy for experimental acid aspiration. *J Surg Res*. 1982;32:168–172.

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Swaminathan A, Naderi N. Pneumonia, aspiration. Available at: http://emedicine.medscape.com/article/807600-overview

A.8. Would you irrigate the bronchial tree with bicarbonate or saline solution?

No. In acid-aspiration pneumonitis, Bannister, Sattilaro, and Otis demonstrated that pulmonary lesions were aggravated by irrigation with sodium bicarbonate, normal saline, and sodium hydroxide. This was explained on the basis that (1) the large volume of fluid served to push the hydrochloric acid deeper into the lungs; (2) mixing of the acid and treatment solution was impossible because of the minute size of the interface; (3) hydrochloric acid probably causes damage within a very short time; (4) if equal volumes of hydrochloric acid (e.g., with a pH value of 1.6) and sodium chloride are mixed, the pH value increases only to 1.8; and (5) neutralization of hydrochloric acid with sodium bicarbonate produces heat, and a thermal burn of the bronchial mucosa may occur.

Bronchial irrigation is indicated only in the obstructive type of aspiration. Five to ten milliliters of normal saline is instilled into the tracheobronchial tree, followed immediately by suction. Bronchial irrigation is preceded and followed by oxygenation. The sequence is repeated until the aspirate fluid is clear.

Bannister WK, Sattilaro AJ, Otis RD. Therapeutic aspects of aspiration pneumonitis in experimental animals. *Anesthesiology*. 1961;22:440–443.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone Elsevier; 2010:2428.

A.9. How would you prevent aspiration during emergency surgery?

The following principles of preoperative preparation are of extreme importance:

- Application of gastric decompression by a wide-bore orogastric tube
- Use of regional anesthesia whenever possible
- Preoperative administration of a clear antacid, such as 30 mL of 0.3-M sodium citrate
- Premedication with anticholinergic agents, such as atropine or glycopyrrolate
- Administration of metoclopramide to stimulate gastric emptying and to increase lower esophageal sphincter tone
- Preoperative administration of an H_2-receptor antagonist or proton inhibitors (pantoprazole sodium) to decrease further secretion of additional acid
- Extubation only when the patient is fully awake

DiSario JA. Future considerations in aspiration pneumonia in the critically ill patient: what is not known, areas for future research, and experimental methods. *JPEN J Parenter Enteral Nutr*. 2002;26(6 suppl):S75–S78; discussion S79.

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Pisegna JR, Martindale RG. Acid suppression in the perioperative period. *J Clin Gastroenterol*. 2005;39(1):10–16.

Smith G, N g A. Gastric reflux and pulmonary aspiration in anaesthesia. *Minerva Anestesiol*. 2003;69(5):402–406.

B. Acute Lung Injury

The patient was extubated in the recovery room. Chest x-ray films showed questionable mottled density in the posterior segments of the right upper lobe. Six hours after being transferred to the floor, she was found to be dyspneic and cyanotic. On auscultation of the chest, significant wheezing was noted and the results of the most recent analysis of arterial blood gases showed the following: pH, 7.26; $Paco_2$, 55 mm Hg; Pao_2, 55 mm Hg; and HCO_3, 20 mEq per L on room air.

B.1. Define acute lung injury (ALI) and acute respiratory distress syndrome (ARDS).

ARDS is the most severe form of ALI. To standardize definitions, a consensus panel of experts developed a set of criteria characterizing ARDS and ALI. The criteria include onset that is acute, bilateral infiltrates on chest radiography, hypoxemia, and no evidence of cardiogenic failure (i.e., pulmonary artery occlusion pressure < 18 mm Hg). Additionally, this group defined hypoxemia in ALI as a Pao_2/Fio_2 ratio of less than 300 mm Hg and selected a threshold ratio of Pao_2/Fio_2 of less than 200 mm Hg for ARDS, reflecting the more severe nature of the disease.

Bernard GR, Artigas A, Brigham KL, et al. The American-European Consensus Conference of ARDS: definitions, mechanisms, relevant outcomes, and clinical trial coordination. *Am J Respir Crit Care Med*. 1994;149:818–824.

Murray JF, Matthay MA, Luce JM, et al. An expanded definition of the adult respiratory distress syndrome. *Am Rev Respir Dis.* 1988;138:720–723.

Putensen C, Wrigge H. Ventilator-associated inflammation in acute lung injury. *Intensive Care Med.* 2000;26:1515–1522.

Tobin MJ. Advances in mechanical ventilation. *N Engl J Med.* 2001;344:1986–1996.

B.2. What are the common causes of ARDS?

ARDS can occur as a result of pulmonary injury arising primarily from lung pathology or secondarily from extrapulmonary processes. These include multiple trauma, massive blood transfusion, septic shock, fat or air embolism, disseminated intravascular coagulation, aspiration pneumonitis, fluid overload, burns, smoke or gas inhalation, and viral and mycobacterial pneumonia. The following conditions are also associated with ARDS: acute renal failure, oxygen toxicity, drug overdose, radiation, immunosuppression, neurogenic pulmonary edema, acute vasculitis, pancreatitis, cardiopulmonary bypass, and Goodpasture syndrome.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia.* 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1222.

Hines RL, Marschall KE. *Stoelting's Anesthesia and Co-existing Disease.* 5th ed. Philadelphia: Churchill Livingstone; 2008:559.

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Tobin MJ. Advances in mechanical ventilation. *N Engl J Med.* 2001;344:1986–1996.

B.3. Describe the pathogenesis of ALI.

The histopathology reveals areas of hyaline membrane, alveolar hemorrhage, increased endothelial and epithelial permeability, and neutrophilic infiltration. Increased permeability allows passage of protein-rich plasma both into the alveolar and into the interstitial spaces, resulting in decreased lung compliance and ineffective gas exchange. As the injury process progresses, dependent lung regions beneath the diseased and edematous lung become collapsed, worsening oxygenation. Additionally, alveolar surfactant content diminishes, and its space becomes filled with fibrin and other cellular materials. Ultimately, a fibroproliferative phase is entered, whereby further destruction of the lungs occurs with varying degrees of collagen deposition and pulmonary fibrosis.

Complement activation may also play a major role in the pathogenesis of ARDS. Activation of the complement cascade through the alternative pathway by endotoxin or lipopolysaccharides results in the production of C5a complement. C5a complement causes microvascular occlusion and pulmonary granulocyte aggregation and embolization. The resultant damage to the endothelium leads to capillary leakage and pulmonary interstitial edema, ultimately producing terminal airway and alveolar edema and collapse. However, studies have shown limitations of the complement-neutrophil theory. Complement activation does not necessarily correlate with the development or severity of ARDS. ARDS can develop in patients with neutropenia, and pulmonary sequestration of neutrophils may not produce lung injury. As a result, the complement-neutrophil theory of ARDS has been expanded to include central roles for additional humoral mediators (such as endotoxin, tumor necrosis factor, interleukins, and thromboxane) and cellular mediators (e.g., the macrophage-monocyte system). The lung in patients with ARDS is now viewed as one of the organs involved in the multiorgan system dysfunction that occurs as a result of the systemic inflammatory

response syndrome. Increased mediator levels are found in bronchoalveolar lavage fluid from patients with ARDS.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia.* 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1222.

Fauci AS, Braunwald E, Kasper DL, et al., eds. *Harrison's Principles of Internal Medicine.* 17th ed. New York: McGraw-Hill; 2008:1680–1684.

Grommes J, Sohnlein O. Contribution of neutrophils to acute lung injury. *Mol Med.* 2010;18. [Epub ahead of print]

Miller RD, ed. *Miller's Anesthesia.* 7th ed. Philadelphia: Churchill Livingstone Elsevier; 2010:2879–2897.

Parsons PE. Mediators and mechanism of acute lung injury. *Clin Chest Med.* 2000;21:467–476.

Raghavendran K, Davidson BA, Mullan BA, et al. Acid and particulate-induced aspiration lung injury in mice: importance of MCP-1. *Am J Physiol.* 2005;289(1):L134–L143.

van Westerloo DJ, Knapp S, van't Veer C, et al. Aspiration pneumonitis primes the host for an exaggerated inflammatory response during pneumonia. *Crit Care Med.* 2005;33(8):1770–1778.

B.4. What are the radiographic findings in ARDS?

The chest radiograph typically shows bilateral, fluffy involvement that initially led clinicians to think the pathology was homogenous. Now, however, pulmonary imaging techniques have provided convincing evidence that the injury is segmental. Although the increased vascular permeability is widespread and homogenous in all lung regions, both total and extravascular lung water is greatest in dependent lung regions. Computed tomography scans of patients with ARDS are several-fold more dense than those of healthy individuals and in severe cases can involve up to 80% of the lung. Based on the findings of Gattinoni et al., the lungs of patients with ARDS may be divided in thirds, wherein one-third represents a completely consolidated, nonventilated region; one-third is healthy with normal ventilation/perfusion matching; and one-third is a region that is hyperinflated with bullae formation. Contrary to previous belief, the compliance of the lung in patients with ARDS is normal for one-third of the lung parenchyma and "stiff" for the rest. The healthy portion is frequently referred to as *baby lung* and is subject to injury because of injudicious assignment of tidal volume. By selecting tidal volume on the basis of body weight (≥10 mL per kg), clinicians have overlooked the important fact that only a small fraction of the total lung in patients with ARDS participates in gas exchange. Therefore, a disproportionate share of the tidal volume will travel to the more compliant areas of the lung, subjecting it to overdistention and injury. Proponents of using lower tidal volume in ALI and in ARDS stress that utilizing a larger tidal volume in such settings is as inappropriate as ventilating an infant's lung with a tidal volume equivalent to that of an adult.

Gattinoni L, Bombino M, Lissoni A, et al. Lung structure and function in different stages of severe adult respiratory distress syndrome. *JAMA.* 1994;271:1772–1779.

Gattinoni L, Pesenti A, Bombino M, et al. Relationships between lung computed tomographic density, gas exchange, and PEEP in acute respiratory failure. *Anesthesiology.* 1988;69:824–832.

Puybasset L, Cluzel P, Chao N, et al. A computed tomography scan assessment of regional lung volume in acute lung injury. *Am J Respir Crit Care Med.* 1998;158:1644–1655.

Rossi UG, Owens CM. The radiology of chronic lung disease in children. *Arch Dis Child.* 2005;90(6):601–607.

B.5. Describe protective-ventilation strategy in ALI and ARDS.

Many investigators have demonstrated a direct association between mechanical ventilation and lung injury that is independent of barotrauma and functionally and histoanatomically identical to injury observed in ARDS. ALI can occur at both low and high lung volumes (Fig. 3.2). At the lower end (below functional residual capacity [FRC]), cyclical opening and closure of alveolar units during tidal breathing may lead to lung injury from generated sheer forces. The regions most subject to this type of injury are at the interface between lung units that are edematous and nonfunctional with regions that are recruitable and mildly affected by the ARDS process. At the other extreme of lung volume, high airway pressure can cause segmental alveolar overdistention.

During the 1990s, use of a protective-ventilation strategy in patients with ALI or ARDS was shown to improve survival rates. Hickling, Henderson, and Jackson were the first to report a 60% reduction in the expected mortality for patients with

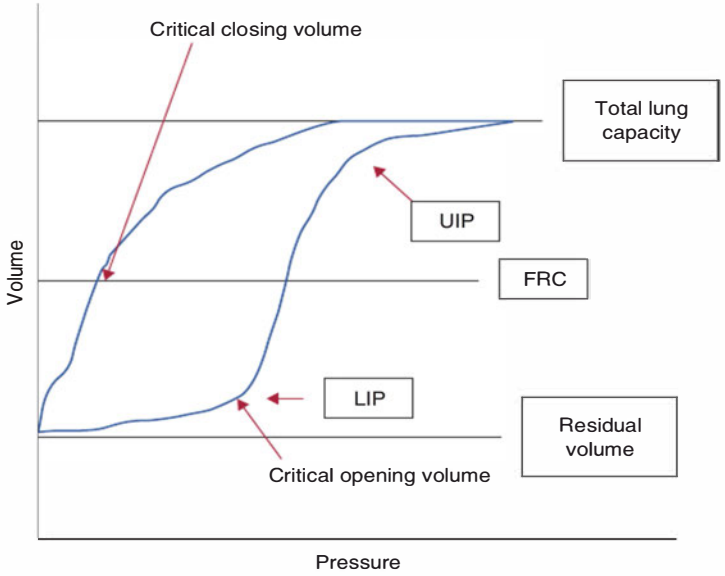

Figure 3.2 Static pressure–volume curve depicting low inflexion point and high inflexion point. On the basis of the concept of a protective-ventilation strategy in acute lung injury (ALI) and acute respiratory distress syndrome (ARDS), there are two critical regions in which pulmonary compliance is very poor. The first region is slightly above the residual volume and denotes a critical opening volume whereby recruitable alveoli have the propensity to collapse during tidal breathing. Cyclic opening and closing of these alveolar units has been implicated as a cause of ventilator-induced lung injury. On a static pressure-volume curve, the determination of this lower inflexion point (LIP) allows the clinician to set the positive end-expiratory pressure (PEEP) to 2 cm H_2O above this critical opening volume to prevent alveolar collapse and promote recruitment. The compliance of the lung markedly improves beyond this point until it reaches higher lung volumes, labeled upper inflexion point (UIP). The ideal tidal volume can be extracted from this exercise as the volume contained between the LIP and the UIP. Similarly, ideal compliance can be derived from the slope of this steep portion (region between LIP and UIP). FRC, functional residual capacity.

ARDS. In a subsequent prospective randomized trial of patients with ARDS treated by a protective lung strategy versus a conventional approach, Amato et al. also demonstrated significant survival improvement in the experimental group. The basic principles of the lung protection strategy include maintenance of lower inspiratory driving pressures (<20 cm H_2O above PEEP); use of lower tidal volumes (6 mL per kg of ideal body weight); acceptance of permissive hypercapnia over higher airway pressures; providing liberal sedation to improve patient-ventilator synchronization; and circumvention of alveolar collapse through judicious use of PEEP. Additional data suggests that early use of neuromuscular blockade to optimize ventilation and oxygenation of patients with ARDS may decrease the number of days on the ventilator and improve mortality without a significant impact on long term muscle function. PEEP maintains the end-expiratory pressure above the lower inflexion point on the static pressure–volume curve of the respiratory system (see Fig. 3.2). This contrasts to management by the conventional approach employing a tidal volume of 12 mL per kg; selection of lowest PEEP to achieve adequate oxygenation; and keeping the arterial carbon dioxide levels between 35 and 38 mm Hg. Fifty-three patients were enrolled in Amato's study (29 were assigned to a protective strategy and 24 were assigned to conventional management). After 28 days, the mortality in the protective-ventilation group was significantly reduced (38% vs. 71%). Further, the rates of weaning from mechanical ventilation were 66% and 29% for the protective-ventilation group and conventional group, respectively.

Following the work of Amato et al., a multicenter study sponsored by the National Institutes of Health (NIH), the ARDS Network, which included 861 patients, reported the same results. Briefly, 432 patients were ventilated with 6 mL per kg of tidal volume, and 429 patients received 12 mL per kg of tidal volume. The mean airway pressures were 25 ± 6 and 33 ± 8 cm H_2O. The trial was stopped prematurely after an interim analysis revealed an overall mortality reduction of 22% in the protective-ventilation group (31% vs. 39%, $P = 0.01$). This trial measured plasma level of interleukin-6 at days 0 through 3 and found it to be markedly reduced in the lower tidal volume group, suggesting fewer systemic inflammatory processes associated with the protective approach.

A recent systematic review of trials of lung protective ventilation strategy in ALI and ARDS found no difference in mortality in patients with ALI, but did find a survival benefit in the subgroup of patients with ARDS.

Acute Respiratory Distress Syndrome Network. Comparison of two fluid-management strategies in acute lung injury. *N Engl J Med.* 2006;354:2564–2575.

Acute Respiratory Distress Syndrome Network. Higher versus lower positive end-expiratory pressures in patients with the acute respiratory distress syndrome. *N Engl J Med.* 2004;351:327–336.

Acute Respiratory Distress Syndrome Network. Pulmonary-artery versus central venous catheter to guide treatment of acute lung injury. *N Engl J Med.* 2006;354:2213–2224.

Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *N Engl J Med.* 2000;342:1301–1308.

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Amato MBP, Barbas CSV, Medeiros DM, et al. Effect of a protective-ventilation strategy on mortality in the acute respiratory distress syndrome. *N Engl J Med.* 1998;338:347–354.

Briel M, Meade M. Higher versus lower positive end expiratory pressure in patients with acute lung injury and acute respiratory distress syndrome: systematic review and meta-analysis. *JAMA.* 2010;303:865–873.

Calfee C, Matthay M. Nonventilatory treatments for acute lung injury and ARDS. *Chest*. 2007;131:913–920.

Fontes ML. Progress in mechanical ventilation. *Curr Opin Anesthesiol*. 2002;15:45–51.

Papazian L, Forel JM, et al. Neuromuscular blockers in early acute respiratory distress syndrome. *N Engl J Med*. 2010;363:1107–1116.

Rivers EP. Fluid-management strategies in acute lung injury: liberal, conservative, or both? *N Engl J Med*. 2006;354:2564–2575.

B.6. Define pulmonary compliance.

Lung compliance is defined as the change in lung volume per unit change in trasmural pressure gradient (i.e., between the alveolus and pleural space). Compliance is measured by adding a known amount of volume to a system and recording the pressure change. The ratio between this volume change and the respective pressure change defines compliance. The reciprocal of this relationship is called *elastance*. The lungs are said to be compliant or noncompliant depending on the pressure change that occurs after a given volume (tidal volume) is delivered. The overall lung compliance is rarely measured during clinical practice; rather, inspiratory pressures (peak airway and plateau pressures) are used to infer the status of overall compliance (lungs and thoracic). In actuality, assessing lung compliance is very difficult because different regions of the lungs exhibit different states of compliance, reflecting the heterogeneity of alveolar compliance. For example, in the upright position, the upper lung fields have the poorest compliance relative to the middle and lower lung segments. Evolutionarily speaking, blood flow is directed to lung regions that have the best compliance (i.e., the dependent regions). As described in the previous section, pulmonary compliance changes as the lung volume is increased from residual volume to total lung volume. At the extremes of volume, compliance becomes reduced. Therefore, the ideal compliance occurs at a lung volume between FRC and the resultant lung volume contributed by a normal tidal volume (7 mL per kg).

Pulmonary compliance changes with aging. Compliance is worse at the extremes of age. In addition, several disease states can compromise pulmonary compliance such as ALI, ARDS, congestive heart failure, barotraumas, neuromuscular disease, obesity, and pregnancy.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 6th ed. Philadelphia: Elsevier Butterworth-Heinemann; 2005:25–33.

C. Mechanical Ventilation

The patient did not improve after receiving 50% oxygen through a face mask. A second arterial blood gas analysis showed the following: pH, 7.25; $Paco_2$, 50 mm Hg; Pao_2, 55 mm Hg; and CO_2 content, 22 mEq per L. The respiratory rate was 40 breaths per minute.

C.1. Interpret the blood gases.

The patient is demonstrating significant signs of respiratory failure. She is hypoxemic, hypercarbic, and dyspneic, and has an acid–base disturbance marked by a combined respiratory and metabolic acidosis. A 10 mm Hg rise in $Paco_2$ should have reduced the pH value by 0.08 (pH = 7.32). Therefore, a comcomitant metabolic acidosis must be present, lowering the pH value to 7.25.

C.2. What is your clinical plan?

Several approaches can be used for the initial management of this patient. A noninvasive approach using PPV by nasal or facemask can be used as a temporizing measure. Bi-level positive airway pressure is typically reserved for patients who are experiencing mild to moderate respiratory failure and who are not at increased risk of aspiration. Given this patient's presentation, the severity of respiratory failure will likely not improve rapidly. In fact, the clinical picture suggests that the patient has suffered ALI resulting in transpulmonary shunting and ineffective ventilation. The safest approach is to electively intubate the trachea and provide mechanical ventilation. Once successfully intubated, sedation can be given to allow for better patient-ventilator synchronization and comfort. If the pulmonary compliance is poor, as is commonly the case in the setting of ALI and ARDS, "deep" sedation may be required as well as muscle relaxation to facilitate gas exchange and to reduce barotrauma.

C.3. What are the criteria for mechanical ventilation?

The physiologic criteria for mechanical ventilation are as follows:

Mechanics

- Respiratory rate of more than 35 breaths per minute
- Vital capacity of less than 15 mL per kg
- Rapid shallow breathing index (respiratory rate/tidal volume–in liters) more than 200 breaths per minute per L

Oxygenation

- Hypoxia - Pa_{O_2} less than 70 mm Hg on face mask oxygen
- Alveolar–arterial oxygen gradient - P_{AO_2}–Pa_{O_2} more than 350 mm Hg on 100% F_{IO_2} or Q_S/Q_T more than 20%

Ventilation

- Hypercarbia - Pa_{CO_2} more than 55 mm Hg, except in patients with chronic hypercarbia
- Increased dead space - V_D/V_T more than 0.60

The trend of values and clinical status is important. The numerical guidelines should not be followed to the exclusion of clinical judgment. Also, frequently, the blood gas analysis results reflect what the patient's status had been at the time the sample was obtained. Depending on the time interval required to perform the analysis and to receive the result, there can be significant exacerbation or resolution in both oxygenation and ventilation, emphasizing the role of clinical judgment.

Fauci AS, Braunwald E, Kasper DL, et al. eds. *Harrison's Principles of Internal Medicine.* 17th ed. New York: McGraw-Hill; 2008:1684–1688.

Hines RL, Marschall K. *Anesthesia and Co-existing Disease.* 5th ed. New York: Churchill Livingstone; 2008:189.

Miller RD, ed. *Miller's Anesthesia.* 7th ed. Philadelphia: Churchill Livingstone Elsevier; 2010:2879–2897.

C.4. Describe the basic modes of mechanical ventilation. Discuss the advantages and disadvantages of pressure-controlled and volume-controlled modes.

Fundamentally, the various modes of mechanical ventilation, both new and old, share the following variables: trigger, control, limit, cycle, and baseline.

Trigger mode

The trigger is the first and most important component of the inspiratory phase, marking the end of exhalation. Examples of triggering mechanisms include time, flow, and pressure. In the nonparalyzed and nonanesthetized state, the patient triggers a mechanical or assisted breath by generating negative transpulmonary pressure that is sensed by the ventilator as a pressure change in the airway (Fig. 3.3). The threshold for triggering a breath (i.e., the set sensitivity) can be altered depending on the clinical setting; however, the greatest challenge in mechanical ventilation is determining the level at which sensitivity pressure should be set (usually at 1 to 2 cm H_2O). If the threshold is set too low, the ventilator will be triggered by any process that causes the airway pressure to surpass the set threshold. These include patient motion, external compression, gastric suctioning, and air leaks in the circuit or in the chest tubes. Conversely, if the threshold is set too high, the work of breathing increases; that is, to trigger every breath, the patient must make a significant effort to overcome the threshold limit for inspiratory flow to occur. At high levels of ventilatory assistance, as much as one-third of the patient's inspiratory efforts may be insufficient to trigger the ventilator. In the setting of acute respiratory failure, the inspiratory effort by the patient is approximately four to six times the normal value. This level of respiratory work frequently causes breath stacking, generating intrinsic PEEP, which in turn

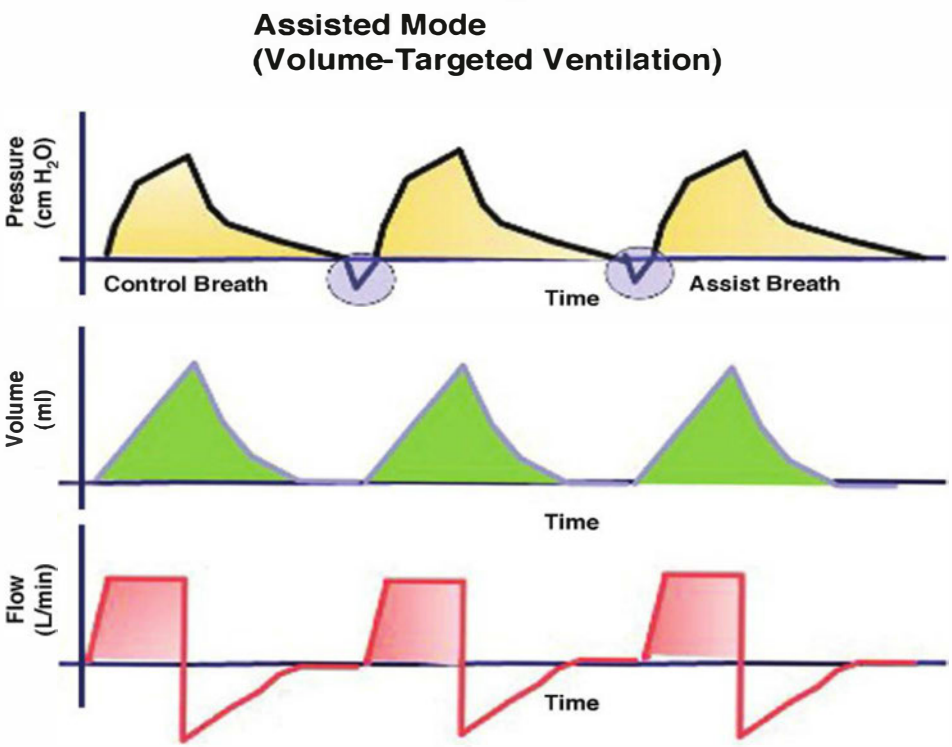

Figure 3.3 Airway pressure with corresponding lung volume and air flow tracings in assisted mode ventilation. The patient triggers a mechanical ventilation by generating negative transpulmonary pressure that is sensed by the ventilator as a pressure change in the airway.

imposes a tremendous burden on inspiratory muscle and if sustained can result in muscle fatigue and cardiopulmonary collapse.

Control mode

The delivered breath can be either pressure regulated (pressure control) or volume targeted (volume control). In the pressure-controlled mode, the amount of volume delivered is inversely related to the resistance encountered. When the resistive forces are low (i.e., normal compliance), the tidal volume for a given pressure will be relatively larger than if compliance were poor. For adults, the recommended upper limit of pressure control is 35 cm H_2O. Higher pressures may directly cause ALI or delay healing of the already injured lung. When the resistive forces are high, the resultant tidal volume may be inadequate for ventilation or oxygenation, even at high levels of inspiratory pressures. Typically, these patients have ARDS, and lower levels of arterial oxygen tension (Pao_2) are tolerated along with higher levels of arterial carbon dioxide tension (permissive hypercapnia).

Volume-controlled mode is the most common control mode used to ventilate patients mechanically. Examples include assist-control ventilation and SIMV. The ventilator will attempt to deliver a preset volume regardless of the pressure generated. For patients with poorly compliant lungs, volume-controlled mode may promote barotrauma and ALI.

Newer ventilators are capable of delivering breaths via a pressure control mode that varies the driving pressure in order to achieve a targeted tidal volume. This mode has the benefit of unrestricted flow during inspiration and automatic adjustment of inspiratory pressure in response to changes in an individual's lung compliance. Clinicians must remember that erratic inspiratory efforts by the patient may prevent the software from calculating an appropriate driving pressure for each breath. In addition, changes in compliance may be missed (especially worsening) as the ventilator will automatically increase the pressure control to get the target volume. One must be mindful to follow the trends in the ventilatory driving pressures and clinical status.

Limit mode

The limit is an essential feature in mechanical ventilation. Its variables include volume, pressure, and flow. The upper and lower limits of these variables should be preselected for each patient and adjusted in a manner consistent with the goals of the protective lung strategy employed.

Cycle mode

As discussed in the previous section, cycling has several variables: time, flow, and pressure. As such, the inspiratory phase and the expiratory phase becomes controlled. The challenge faced is in synchronizing the machine's cycling of inspiration and exhalation with the patient's "neural" respiratory cycle. Although pressure, flow, and time can be used to affect cycling, the manipulation of one or all three variables, both intrabreath and interbreath, to coincide precisely with the demands of the patient is virtually impossible (Fig. 3.4).

Baseline mode

The baseline variable is the function that is controlled during exhalation and generally indicates the level of PEEP.

Briel M, Meade M. Higher versus lower positive end expiratory pressure in patients with acute lung injury and acute respiratory distress syndrome: Systematic review and meta-analysis. *JAMA.* 2010;303:865–873.

Chatburn RL. Understanding mechanical ventilators. *Expert Rev Respir Med.* 2010;6:809–819.

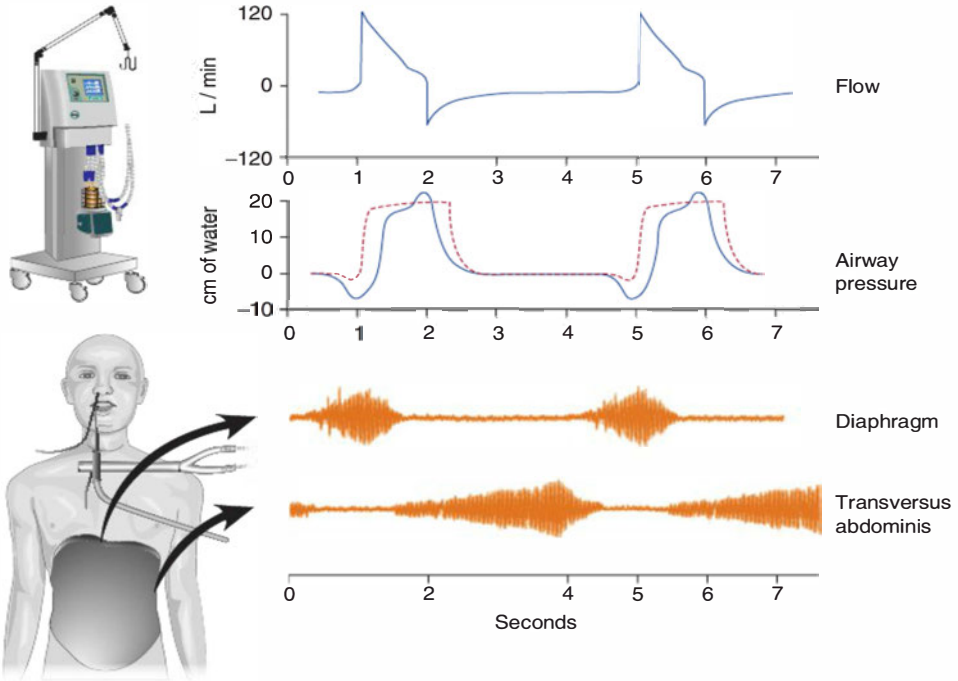

Figure 3.4 Activation of expiratory muscle during a mechanical inspiratory cycle. The airway flow, pressure, and electromyogram recording of two mechanically assisted respiratory cycles are illustrated. The start of inspiration is reflected by diaphragmatic activity that begins before the commencement of the inspiratory flow or airway pressure. The diaphragm stops contracting, marking the end of inspiratory effort. The expiratory muscle activity begins with contraction of the transversus abdominis muscle **(lower panel)**; however, the ventilator continued to deliver inspiratory flow while the patient was attempting to exhale. This illustrates a common problem with all ventilation modes that cannot fully adapt and synchronize with the patient's neuronal timing of inspiration and expiration. In the case mentioned earlier, the ventilator's inspiratory time exceeded the patient's inspiratory cycle, resulting in dyssynchrony and in some instances high airway pressure, predisposing to barotrauma. (From Tobin MJ. Advances in medical ventilation. *N Engl J Med.* 2001;344:1986–1996, with permission.)

Fauci AS, Braunwald E, Kasper DL, et al., eds. *Harrison's Principles of Internal Medicine.* 17th ed. New York: McGraw-Hill; 2008:1684–1688.

Fontes ML. Progress in mechanical ventilation. *Curr Opin Anesthesiol.* 2002;15:45–51.

Hess D, Branson R. Ventilators and weaning modes. *Respir Care Clin N Am.* 2000;6:407–435.

Miller RD, ed. *Miller's Anesthesia.* 7th ed. Philadelphia: Churchill Livingstone Elsevier; 2010:2879–2897.

Tobin MJ. Advances in mechanical ventilation. *N Engl J Med.* 2001;344:1986–1996.

C.5. What control mode would you select for this patient?

For adult patients, volume-controlled mode most often is chosen for ventilatory management. Examples include assist-control ventilation, SIMV, and PSV. A targeted

tidal volume is selected and the ventilator will attempt to deliver this volume regardless of the pressure generated. If the resistance to ventilation is great, the pressure change can be excessive, resulting in barotrauma and ALI. Occasionally, the pressure increase is acute, reflecting some reversible condition, such as mucous plugging, bronchospasm, and patient anxiety. These conditions can be treated appropriately without having to switch to a different ventilatory mode. Alternatively, patients with ALI may have very poor compliance for which volume-controlled mode may be ineffective or prohibitive.

Some alternative modes of mechanical ventilation combine pressure control that is volume compensated or vice versa. Examples include pressure-regulated volume-controlled ventilation, proportional assist ventilation, adaptive support ventilation, and many other combinations of volume control, volume support, pressure support, and pressure control. These alternative modes attempt to improve patient comfort and synchronization with the ventilator. Older modes were overly simplistic, and incorrect assumptions were made regarding the role of ventilatory assistance. The concept was to make the ventilator the "boss" and allow it to drive the respiratory cycles. The important insight gained from today's clinical research is that the ventilator should be a "helper" aimed at assisting the patient in a manner determined by the patient.

Briel M, Meade M. Higher versus lower positive end expiratory pressure in patients with acute lung injury and acute respiratory distress syndrome: systematic review and meta-analysis. *JAMA.* 2010;303:865–873.

Chatburn RL. Understanding mechanical ventilators. *Expert Rev Respir Med.* 2010;6:809–819.

Esteban A, Anzueto A, Alia I, et al. How is mechanical ventilation employed in the intensive care unit? An international utilization review. *Am J Respir Crit Care Med.* 2000;161:1450–1458.

Tobin MJ. Mechanical ventilation. *N Engl J Med.* 1994;330:1056–1061.

C.6. What initial ventilator settings will you prescribe for this patient (tidal volume, respiratory frequency, inspiratory oxygen fraction, etc.)?

Initially, an attempt will be made to ventilate the patient with a volume-controlled mode. The tidal volume will be set at 5 to 8 mL per kg, respiratory frequency at 10 breaths per minute, F_{IO_2} of 70%, PEEP of 10 cm H_2O. The limits for alarming will be standard. After this initial setting, an arterial blood gas analysis should be performed to determine the adequacy of ventilation and oxygenation. Should lung compliance be poor, large tidal volumes must be avoided, which will predispose the lungs to barotrauma. The patient should be adequately sedated, and both the patient and the ventilator should be examined to rule out correctable causes of elevated inspiratory pressures. Alternatively, a pressure-controlled mode can be selected to ensure the driving pressure (plateau or mean airway pressure) does not exceed 35 cm H_2O. The PEEP level should be adjusted to improve oxygenation. A Pao_2 level of more than 60 mm Hg is acceptable, and the level of $Paco_2$ can rise in excess of 60 or 70 mm Hg (permissive hypercapnia). Treating the ensuing acidemia, particularly, respiratory acidemia no longer is recommended, unless the pH value becomes less than 7.20. The use of sodium bicarbonate is reserved for profound acidemia. Once administered, this agent is chemically converted to byproducts that include H_2O and CO_2. The latter can diffuse easily through the cell membrane to make the intercellular milieu more acidotic.

Chatburn RL. Understanding mechanical ventilators. *Expert Rev Respir Med.* 2010;6:809–819.

C.7. Describe the potential hemodynamic effects of positive pressure ventilation (PPV).

During spontaneous inspiration, air is delivered to the lungs by generating a pressure gradient between pleural (negative pressure) and atmospheric pressures (1 atmospheric pressure). During exhalation, the reverse process occurs and air is expelled as pleural pressure increases (never positive) and the rib cage recoils, returning lung volume to FRC. The hemodynamic consequence of physiologic breathing is minor but is associated with alterations in systemic blood pressure. For example, during inspiration, blood flow to the right ventricle is promoted and blood flow to the left side of the heart is diminished. This results in a decrease in stroke volume and systemic systolic pressure (approximately 5 to 10 mm Hg). In contrast, during positive pressure inspiration, the ventilator applies positive pressure to overcome alveolar pressure. Overall, transthoracic pressure increases, impeding or diminishing venous return to the heart. Both the right and the left ventricular output can decrease depending on the thoracic compliance, intravascular volume status, and biventricular function; that is, PPV will cause a decrease in cardiac output and blood pressure when the overall lung compliance is poor, the intravascular volume is inadequate, and/or ventricular function is compromised.

The hemodynamic consequences of both spontaneous pressure ventilation and PPV may be profound and may have opposite effects on cardiovascular stability in different patient populations. Therefore, no firm rules apply about the specific response that will be seen in all patients and under all conditions. Some generalities, however, are probably reasonable. In patients with markedly increased work of breathing, hypervolemia, or impaired left ventricular pump function, the institution of mechanical ventilatory support can be life saving because of its ability to support the cardiovascular system, independent of any beneficial effects that mechanical ventilation may have on gas exchange. In patients with decreased pulmonary elastic recoil, increased pulmonary vascular resistance, hypovolemia, or airflow obstruction, the institution of mechanical ventilatory support may induce cardiovascular instability, which if not corrected can lead to total cardiovascular collapse.

The initiation of intermittent positive pressure ventilation (IPPV) is associated with a decrease in cardiac output and in arterial blood pressure in patients without significant lung consolidation. Cardiac output and stroke volume decrease as the peak airway pressure increases. There is also a decrease in cardiac output with increasing inspiratory/expiratory ratios. IPPV increases intrathoracic pressure, resulting in decreased venous return and cardiac output. Patients with healthy lungs behave differently from patients with significant cardiopulmonary disease. When pulmonary compliance decreases, the transmission of airway pressure to intrathoracic pressure decreases. Patients with more rigid lungs can tolerate higher airway pressures.

IPPV decreases transmural pulmonary artery pressure without a change in pulmonary vascular resistance. The systemic vascular resistance increases slightly when IPPV is begun. The decrease in cardiac output during IPPV is rarely of any clinical significance because it is compensated by an increase in peripheral vascular resistance in nonanesthetized patients. When patients are hypovolemic, the decrease in blood pressure can be significant.

Chatburn RL. Understanding mechanical ventilators. *Expert Rev Respir Med*. 2010;6:809–819.

Pinsky MP. Cardiovascular effects of ventilatory support and withdrawal. *Anesth Analg*. 1995;79:567–576.

C.8. What are the adverse effects of mechanical ventilation?

Physiologic complications

- Decreased cardiac output resulting from increased intrathoracic pressure
- Respiratory alkalosis from hyperventilation
- Increased venous admixture ($\dot{Q}s/\dot{Q}T$) from prolonged low tidal volume ventilation

Pulmonary complications

- Infection
- ALI
- Barotrauma/pneumothorax, mediastinal, interstitial, and subcutaneous emphysema in 10% to 15% of adults
- Oxygen toxicity if the inspired oxygen concentration is more than 60%
- Atelectasis caused by immobilization and ineffective humidification

Complications from endotracheal intubation

- Endobronchial intubation, kinking, or obstruction, cuff leak
- Nasal damage from nasal intubation, epistaxis, fractured turbinates, septal perforation, partial loss of alae nasi, nasal synechiae
- Laryngeal damage and edema, vocal cord paresis and granulomas, laryngotracheal membranes, subglottic fibrotic stenosis
- Tracheal damage and tracheal erosion, tracheoesophageal fistula, tracheomalacia, tracheal stenosis
- Complications from mechanical device malfunction

Byrd R Jr, Kosseifi S, Roy T. Ventilation, mechanical. Available at: http://emedicine.medscape.com/article/304068-overview

Chatburn RL. Understanding mechanical ventilators. *Expert Rev Respir Med.* 2010;6:809–819.

Hines RL, Marschall K. *Stoelting's Anesthesia and Co-existing Disease.* 5th ed. New York: Churchill Livingstone; 2008:485.

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D. Therapeutic Approaches for Ventilatory Support

After intubation and mechanical ventilation, the oxygenation did not improve. On F_{IO_2}, 0.7, the arterial blood gas analysis showed the following: pH, 7.30; P_{aCO_2}, 40 mm Hg; P_{aO_2}, 57 mm Hg; and CO_2 content, 18 mEq per L.

D.1. What factors determine oxygen delivery?

Oxygen delivery is dependent on blood flow (cardiac output) and the content of oxygen carried in blood (hemoglobin and dissolved oxygen). The actual amount is reflected by the following formula:

$$\text{Oxygen delivery} = CO \times [(1.34 \times Hgb \times Sa_{O_2}) + (0.0031 \times Pa_{O_2})]$$

where *CO* is cardiac output; *Hgb,* hemoglobin content in blood; Sa_{O_2}, percent arterial oxygen saturation; and Pa_{O_2}, partial pressure of oxygen dissolved in blood.

Based on this formula, oxygenation can be improved by several modalities. First, it is important to determine where the physiologic derangement lies. If the cardiac output is inadequate, the appropriate therapy should be to improve the elements of cardiac output (rate and rhythm, preload, contractility, and afterload); next, should the hemoglobin content be too low, the patient should undergo a transfusion with red blood cells; last, oxygen delivery to the lungs and uptake should be maximized. The latter can be accomplished by increasing the inspired oxygen concentration, increasing the level of PEEP, and by other maneuvers that will improve ventilation/perfusion matching and decrease intrapulmonary shunting (e.g., chest physiotherapy, prone position, bronchodilators, and diuresis).

Ginosa Y, Pizov R, Sprung C. Arterial and pulmonary artery catheters. In: Parrillo J, Bone R, eds. *Critical Care Medicine, Principles of Diagnosis and Management*. St. Louis: Mosby-Year Book; 1995:27–49.

D.2. How will you treat the hypoxemia?

The arterial blood gas analyses suggest that the patient is hypoxemic but is adequately ventilated and has a component of metabolic acidosis. As discussed previously, it is *not* appropriate to correct this level of metabolic acidosis with sodium bicarbonate or to attempt to hyperventilate the patient and induce respiratory alkalosis. The underlying problem producing the hypoxemia is lung injury from the aspiration pneumonitis, whose effect has led to significant intrapulmonary shunting. The F_{IO_2} is set at 0.7. The most appropriate maneuver is to increase the PEEP level, ensure good patient-ventilator synchronization (i.e., the patient is not fighting the ventilator), and avoid excessive tidal volumes or inspiratory driving pressures. Other ventilatory modalities that can be applied include inverse-ratio ventilation, pressure-controlled ventilation, prone position, use of NO, jet ventilation, and partial liquid ventilation (PLV).

D.3. What are the major factors governing oxygen toxicity?

Oxygen toxicity is governed by the duration of exposure, the partial pressure of oxygen, and the susceptibility of the individual to pulmonary oxygen injury. The degree of toxicity is related to the partial pressure, but not to the percentage of oxygen inspired, as demonstrated during U.S. space flights, where astronauts tolerate 100% oxygen for 2 to 4 weeks at a tension of 250 mm Hg. Systemic oxygen toxicity is related to arterial oxygen tension, whereas pulmonary oxygen toxicity depends on alveolar oxygen tension. Retrolental fibroplasia (retinopathy of prematurity) in the premature neonate has been reported after exposure to Pa_{O_2} at more than 80 to 150 mm Hg for a few hours. Pulmonary toxicity can develop after prolonged exposure to oxygen at concentrations between 0.5 and 1.0 atmospheres. It must be emphasized that the adult patient can generally tolerate 1 atmosphere of oxygen partial pressure for at least 24 hours. Moreover, there is no evidence that clinically relevant pulmonary oxygen toxicity occurs in humans at inspired partial pressures less than 0.5 atmosphere. Lastly, no patients should ever experience life-threatening levels of hypoxemia to avoid possible oxygen toxicity.

Deneke SM, Fanburg BL. Normobaric oxygen toxicity of the lung. *N Engl J Med.* 1980;303:76–86.

Frank L, Massaro D. Oxygen toxicity. *Am J Med.* 1980;69:117.

Lumb AB. *Nunn's Applied Respiratory Physiology.* 6th ed. Philadelphia: Elsevier Butterworth-Heinemann; 2005:348–358.

D.4. What is the mechanism of oxygen toxicity?

The free-radical theory of oxygen toxicity proposed in the early 1960s has garnered a great deal of recent experimental support and is now accepted as the most probable molecular-level explanation for oxygen toxicity. Various highly reactive and potentially cytotoxic free-radical products of oxygen are generated metabolically in the cell. These short-lived O_2 metabolites, including superoxide anion (O_2^-), hydroxyl radical (OH), hydrogen peroxide (H_2O_2), and singlet oxygen (O^-), have been shown to be capable of effects such as inactivation of sulfhydryl enzymes, interaction with and disruption of DNA, and peroxidation of unsaturated membrane lipids with resultant loss of membrane integrity. The cell is also equipped with an array of antioxidant defenses, including the enzymes superoxide dismutase, catalase, glutathione peroxidase, vitamin E, and ascorbate. Under hyperoxia, the intracellular generation and influx of free radicals is believed to increase markedly and may overwhelm the detoxifying capacity of the normal complement of antioxidant defenses, with resultant cytotoxicity.

The pathology of oxygen toxicity is nonspecific and consists of atelectasis, edema, alveolar hemorrhage, inflammation, fibrin deposition, and thickening and hyalinization of alveolar membranes. There are exudative and proliferative phases. Capillary endothelium is damaged early and plasma leaks into interstitial and alveolar spaces. Pulmonary surfactant may be altered. Type I alveolar lining cells are injured early, and bronchiolar and tracheal ciliated cells can be damaged by 80% to 100% oxygen. Resolution of exudative changes, hyperplasia of alveolar type II cells, fibroplastic proliferation, and interstitial fibrosis occur with recovery or with the development of tolerance to oxygen. Total resolution is possible if the initial hyperoxia is not overwhelming.

Deneke SM, Fanbarg BL. Normobaric oxygen toxicity of the lung. *N Engl J Med.* 1980;303:76–86.

Frank L, Massaro D. The lung and oxygen toxicity. *Arch Intern Med.* 1979;139:347–350.

Freeman BA, Crapo JD. Free radicals and tissue injury. *Lab Invest.* 1982;47:412.

Lumb AB. *Nunn's Applied Respiratory Physiology.* 6th ed. Philadelphia: Elsevier Butterworth-Heinemann; 2005:348–358.

D.5. What are your criteria to start positive end-expiratory pressure (PEEP)?

The role of PEEP in mechanical ventilation is evolving. Previously, it was reserved for patients who had significant pulmonary pathology and hypoxemia. Either in apparently healthy lungs or in disease lungs, there can be significant heterogeneity in alveolar compliance and ventilation. Therefore, at normal levels of PEEP (physiologic), while in the supine position, alveolar components can collapse during tidal breathing, particularly, when there exist underlying comorbid states (e.g., ALI, ARDS, chronic obstructive pulmonary disease [COPD], congestive heart failure, obesity, and general anesthesia). To prevent cyclical closure of alveolar units and to ensure that the lung volume is maintained at or slightly above FRC, PEEP should be instituted accordingly. One should not wait for physiologic or laboratory evidence of inadequate gas exchange to initiate PEEP. Five to 10 cm H_2O is often sufficient and is not associated with hemodynamic disturbances. In the setting of ALI and ARDS, application of PEEP is essential for achieving adequate oxygenation.

Briel M, Meade M, Mercat A, et al. Higher vs lower positive end-expiratory pressure in patients with acute lung injury and acute respiratory distress syndrome: systematic review and meta-analysis. *JAMA*. 2010;303(9):865–873.

Byrd R Jr, Kosseifi S, Roy T. Ventilation, mechanical. Available at: http://emedicine.medscape.com/article/304068-overview

Chatburn RL. Understanding mechanical ventilators. *Expert Rev Respir Med*. 2010;6:809–819.

Gattinoni L, Caironi P, Cressoni M, et al. Lung recruitment in patients with the acute respiratory distress syndrome. *N Engl J Med*. 2006;354(17):1775–1786.

Mercat A, Richard JC, Vielle B, et al., for the Expiratory Pressure (Express) Study Group. Positive end-expiratory pressure setting in adults with acute lung injury and acute respiratory distress syndrome: a randomized controlled trial. *JAMA*. 2008;299(6):646–655.

Petrucci N, Iacovelli W. Lung protective ventilation strategy for the acute respiratory distress syndrome. *Cochrane Database Syst Rev*. 2007.

D.6. How does PEEP improve arterial oxygenation?

The mechanism is related to an increase in the FRC and redistribution of extravascular lung water. The FRC expands linearly with increases in the end-expiratory pressure, usually at a rate of 400 mL or more for each 5 cm H_2O of end-expiratory pressure; however, recruitment of alveolar units is both variable and unpredictable in patients with ARDS. This increase in FRC represents alveoli that remain open and available for gas exchange during all phases of the respiratory cycle. The increase in FRC improves the relationship between FRC and closing capacity and therefore decreases intrapulmonary shunt or venous admixture.

PEEP therapy changes the distribution of interstitial lung water but does not directly decrease lung water. PEEP facilitates the movement of water from the less compliant interstitial spaces (between the alveolar epithelium and capillary endothelium, where gas exchange occurs) to the more compliant interstitial spaces (toward the peribronchial and hilar areas). This redistribution of interstitial lung water improves oxygen diffusion across the alveolar-capillary membrane, resulting in increased arterial oxygenation. Approximately 25% of patients with ARDS are unresponsive to increases in PEEP as measured by an increase in Pao_2.

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Phoenix SI, Paravastu S, Columb M, et al. Does a higher positive end expiratory pressure decrease mortality in acute respiratory distress syndrome? A systematic review and meta-analysis. *Anesthesiology*. 2009;110(5):1098–1105.

Solsona JF, Diaz Y, Vazquez A, et al. A pilot study of a new test to predict extubation failure. *Crit Care*. 2009;13(2):R56.

D.7. How would you determine the best PEEP and the optimal PEEP?

Suter, Fairley, and Isenberg described best conventional PEEP in 1975. The best PEEP is defined as the level of PEEP with the highest oxygen transport, which is the product of cardiac output and oxygen content. This PEEP correlates with the highest

total respiratory compliance, the highest mixed venous oxygen tension, and the lowest V_D/V_T. Arterial oxygen tension and intrapulmonary shunt are not good indicators of the best conventional PEEP. They continue to improve even after this level has been reached. Oxygen transport decreases after the best PEEP is reached, because the cardiac output decreases.

Civetta, Barnes, and Smith described optimal high PEEP in 1975. It is defined as the level of PEEP with the lowest intrapulmonary shunt and without compromising cardiac output. The PEEP used in this report is high, more than 25 cm H_2O, whereas the PEEP in the article by Suter, Fairley, and Isenberg is more conventional, ranging from 5 to 20 cm H_2O. However, the concept of best or optimal PEEP has evolved over the years. More recently, the endpoint for PEEP application is the lowest level of PEEP that provides an adequate Pa_{O_2} at an F_{IO_2} of less than 0.5. Increasing PEEP beyond this level to obtain optimum values for various other endpoints, such as the production of maximum oxygen transport, maximum static pulmonary compliance, shunt less than 15% to 20%, minimal arterial end-tidal Co_2 gradient, decreased mixed venous oxygen tension, and minimum F_{IO_2} will not be clinically helpful and may be harmful.

Branson RD, Johannigman JA. What is the evidence base for the newer ventilation modes? *Respir Care*. 2004;49(7):742–760.

Civetta JM, Barnes TA, Smith LO. Optimal PEEP and intermittent mandatory ventilation in the treatment of acute respiratory failure. *Respir Care*. 1975;20:551–557.

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Solsona JF, Diaz Y, Vazquez A, et al. A pilot study of a new test to predict extubation failure. *Crit Care*. 2009;13(2):R56.

Suter PM, Fairley HB, Isenberg MD. Optimum end-expiratory airway pressure in patients with acute pulmonary failure. *N Engl J Med*. 1975;292:284–288.

D.8. What are the cardiovascular effects of PEEP?

The cardiovascular effects of PEEP depend on the severity of respiratory failure, the level of PEEP, the intravascular volume, the contractility of the heart, and the pulmonary vasculature. In healthy subjects without respiratory failure, PEEP decreases cardiac output mainly because of increased intrathoracic pressure resulting in decreased venous return. PEEP also causes pulmonary parenchymal overdistention, which makes the lung come in close contact with the left ventricle, changing compliance and interfering with ventricular function. In addition, PEEP increases pulmonary pressure and resistance, resulting in right ventricular dilation, which causes an intraventricular septum shift toward the left ventricle. The leftward septal shift decreases left ventricular diastolic filling, resulting in decreased stroke volume and cardiac output. Also, unilateral pulmonary hyperinflation may initiate neural reflexes, resulting in a decreased cardiac output and heart rate. Moreover, humoral depression of myocardial contractility may also be observed. The aforementioned deleterious effect of PEEP is more apparent in individuals with limited cardiovascular reserve. Although PEEP is applied only at the end of expiration, in actuality, the alveolar and transpulmonary pressures are highest during inspiration (driving pressures exceeding 20 to 30 cm H_2O in some patients) and are associated with the greatest negative hemodynamic effects.

In persons with respiratory failure, PEEP, up to optimum levels, usually increases or does not change cardiac output because of an increase in oxygenation with resultant improvement of cardiac performance. Cardiac output decreases when PEEP exceeds the individual's optimum PEEP. Hypotension during PEEP therapy may be exacerbated by hypovolemia.

In patients with underlying left ventricular failure and left ventricular diastolic pressure of more than 18 mm Hg, PEEP may increase cardiac output by increasing coronary arterial oxygen content, augmenting systolic function, or reducing venous return. The decreased venous return may produce a shift in the Starling curve to filling pressures associated with better myocardial function.

Pinsky MP. Cardiovascular effects of ventilatory support and withdrawal. *Anesth Analg.* 1995;79:567–576.

Robotham JL, Lixfeld W, Holland L, et al. The effects of positive end-expiratory pressure on right and left ventricular performance. *Am Rev Respir Dis.* 1980;121:677–683.

D.9. What is pressure-support ventilation (PSV)? Discuss its advantages.

PSV is pressure-limited, flow-controlled PPV during which each spontaneous inspiratory effort is assisted by mechanically maintaining a predetermined inspiratory pressure plateau throughout inspiration. Whereas PSV is most often flow cycled, both pressure and time can be secondary cycling mechanisms. That is, pressure support can cycle to the exhalation phase when flow decelerates to a ventilator-determined level or to a pressure-determined level and/or when the inspiratory time has reached a predetermined level. PSV can be used for patients who are breathing completely spontaneously or who are being supported with IMV (Fig. 3.5), and it can be used for patients receiving CPAP.

PSV, which is an adjunct form of ventilatory support, is controlled with a microprocessor incorporated into the mechanical ventilator's circuit. When the patient makes the initial inspiratory effort, a very sensitive pressure transducer detects the slight negative pressure change and application of a constant support pressure is begun. Pressure is applied continuously throughout inspiration at the value selected by the operator.

The advantages of PSV are as follows:

- Achieving larger tidal volumes with lower airway pressures
- Decreasing work of breathing
- Improving spontaneous breathing patterns, including decreased respiratory rate, longer expiratory phase, and better synchrony with mechanical ventilation
- Promoting weaning from mechanical ventilation because of decreased respiratory muscle fatigue

Although theoretic advantages and safety of the mode in appropriately monitored patients support its use, few clinical studies have documented the efficacy of PSV.

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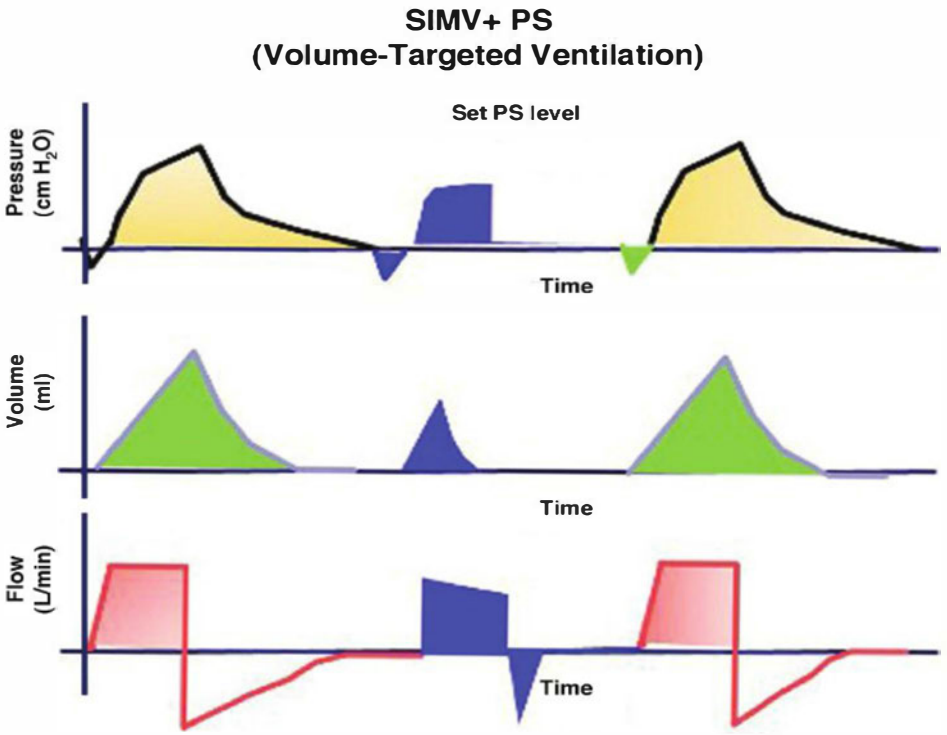

Figure 3.5 Airway pressure with corresponding lung volume and air flow tracings in spontaneous intermittent mandatory ventilation (SIMV) with pressure support (PS).

D.10. Describe the rationale for prone-position ventilation and its effect on oxygenation.

The concept of improving oxygenation and gas exchange in patients with ARDS was proposed more than 30 years ago. The mechanisms for improvement in oxygenation in the prone position are unclear, and whether such physiologic benefit alters outcome is equally unknown. For gas exchange to improve, several respiratory processes must occur: (1) better matching of ventilation and perfusion in those lung regions affected by either too little perfusion but normal ventilation or normal perfusion but inadequate ventilation; (2) improvement in pulmonary diffusion capacity of oxygen and carbon dioxide (i.e., reduced interstitial edema and inflammation); (3) improvement in mobilization and delivery of these gases from the tissues to the lungs (better cardiac output and end-organ function); and (4) reduction in ventilator-induced lung injury in the prone position as compared with supine. In ARDS, the whole lung is affected by endothelial and epithelial hyperpermeability with resulting edema. In the supine position, dependent lung regions are subjected to a relatively greater regional pleural pressure gradient secondary to the forces of gravity acting on the ribcage, the diaphragm, the abdomen, the heart, and the mediastinal structures. Such increases in transpulmonary pressures overstretch normal alveoli, cause epithelial and endothelial disruption, and induce a state of pulmonary edema. Studies of animal models of ALI have shown that while in the supine position, high levels of PEEP are required to

maintain the injured and surfactant-depleted alveoli open. Failure to do this promotes ventilator-related lung injury. Additionally, perfusion of these dependent regions may be reduced from regional compression by the weight of the edematous upper lung units and from the effects of hypoxic pulmonary vasoconstriction. In contrast, positioning the patient prone allows for a more uniform gravitational gradient for alveolar ventilation and redistribution of alveolar ventilation to dorsal lung regions. Several other processes may account for the observed improvement in physiologic parameters in the prone position:

- The airway orientation is such that it tends to promote drainage of airway liquids toward the airway opening while in prone position and toward the dorsal regions when lying supine
- Redistribution of perfusion along a gravitational gradient to less injured lung regions
- Increased FRC
- Change in regional diaphragm motion

Pelosi et al. measured the change in thoracoabdominal compliance in the supine versus the prone position and compared this to changes in oxygenation. They found a direct correlation between improvement in compliance in the prone position and improvement in oxygenation that was most likely attributed to positioning the more rigid ribcage and vertebrae in the superior position while splinting the mobile anterior chest by the mattress. This maneuver favored redistribution of ventilation to the dorsal lung segments and alveolar recruitment.

Voggenreiter compared the effects of intermittent prone ventilation in 22 patients (11 of whom had severe and moderate posttraumatic lung injury and 11 had ARDS). Statistically significant improvements in respiratory parameters were observed in the prone position relative to the supine position for the following variables: (1) oxygenation; (2) $P_{AO_2} - P_{aO_2}$ and $\dot{Q}_S/\dot{Q}_T$; (3) total static lung compliance; and (4) reduction in pulmonary densities.

Prone position can improve oxygenation in patients with ARDS, and it may decrease the incidence of ventilator-associated pneumonia. The benefit appears to most in a subgroup of the most severely ill patients, in whom, it may it also lower mortality.

A recent meta-analysis found an improvement in hypoxia and decreased mortality in patients with ARDS who were ventilated in the prone position, albeit with a higher risk of complications, including pressure ulcers, endotracheal tube obstruction and chest tube dislodgement. In summary, prone position ventilation may improve oxygenation in 60% to 70% of people. Because not everyone will respond, a brief test of the prone position is recommended to assess responsiveness. The optimal duration of this treatment, and the repeat benefit of successive trials, is not currently known.

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D.11. How is liquid ventilation accomplished?

Kylstra, who demonstrated that salt solutions could be saturated with oxygen at high pressures, first introduced the concept of fluid breathing in the 1960s. In 1966, Leland Clark uncovered that both oxygen and carbon dioxide were soluble in fluorocarbon liquids. The earlier methods of liquid ventilation with fluorocarbons met limited success as a result of impurities and chemical compositions of the fluorocarbons that caused ALI. Advances in perfluorocarbon (PFC) technology, however, have led to the development of improved generations of oxygen carriers that incorporated nontoxic substances. The PFC compounds are inert organic chemicals produced by replacement of fluorine for hydrogen in specific sites within the carbon chain. These agents do not undergo metabolism in the body and are eliminated through the pulmonary, gastrointestinal, and renal systems.

The proposed mechanisms for both improvement in oxygenation and hastening of recovery from ALI include a high solubility coefficient for oxygen and carbon dioxide relative to hemoglobin and a density that is twice that of water. As such, replacement of the FRC by PFC eliminates the alveolar membrane-air-liquid interface, reduces surface tension in the surfactant-depleted lung, and physically maintains the alveoli open. Because of its high density, it tends to gravitate toward the more dependent lung region that is most affected by lung edema and ALI. This effect stabilizes alveolar units in these regions and aids in alveolar recruitment. The use of PLV with PFC may alter regional blood flow by diverting blood from dependent to nondependent lung regions, thereby improving ventilation/perfusion matching (i.e., fluid PEEP). An additional benefit of PLV is the displacement of alveolar proteinaceous edema, inflammatory cells, debris, and other mediators from the alveolar spaces that are less dense.

Several clinical trials investigating the effect of PFC for PLV have shown a dose-dependent improvement in oxygenation. Leach et al. studied the efficacy of PLV using perflubron—an 8-carbon PFC—in 13 premature infants with severe ARDS in whom conventional therapy using various modalities, including surfactant replacement, had failed. An amount of PFC equaling the infant's FRC was infused endotracheally while standard mechanical ventilation was maintained. Within 1 hour after installation of PFC, the Pao_2 increased by 138% and the dynamic compliance improved by 61%. Whereas the duration of PLV was 24 to 72 hours and no direct complications occurred during the trial, the overall mortality rate was 50%. In 2001, Schuster et al. investigated whether or not the distribution of PFC in PLV is inhomogeneous, resulting in either inadequate improvement or deterioration in oxygenation, particularly during the first 24 hours after initiation of PLV. Inhomogeneity in distribution may arise from regional obstruction of airway components by (1) cellular debris, edema, and inflammatory factors; (2) local destruction of lung parenchyma; and (3) regional uptake of the PFC by blood. In this study, the chest radiograph of 16 patients who had received PLV for 48 hours were reviewed. The best predictor of inhomogeneous filling was the initial dose of PFC (10 mL per kg as compared with 20 mL per kg). Although other investigators have shown a dose-dependent improvement in oxygenation, several others have confirmed the findings of Schuster et al.

PLV has been combined with several ventilatory approaches to maximize oxygen delivery. Suh et al. showed, in an animal model of ALI, that PLV has a dose-dependent increase in Pao_2 with PEEP or proning as compared with volume-controlled mechanical ventilation mode. Additionally, lung histology revealed significantly less hyaline membrane formation in the PLV group, suggesting that this modality of ventilation allows the lungs to heal after an acute injury process. Relative to lungs from conventionally ventilated animals, similar histologic findings have been described whereby

the use of PLV resulted in less alveolar hemorrhage, decreased lung fluid accumulation, and diminished neutrophilic infiltration. This anti-inflammatory benefit may be attributed to the mechanical lavage of alveolar debris by the PFC and by a direct effect on alveolar macrophages. Despite these proven benefits, the use of PFC for PLV remains investigative for management of ARDS and ALI. Additional larger randomized clinical trials addressing the efficacy and safety of PLV need to be performed before any definitive recommendation can be made.

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D.12. What are the indications and contraindications for extracorporeal membrane oxygenation (ECMO)? How many ways can it be used? What are its results?

ECMO should be used for patients in severe acute respiratory failure with potentially reversible lung disease, who are dying of severe hypoxemia despite maximal conventional ventilatory care (e.g., tracheal intubation, mechanical ventilation with high PEEP, diuresis, chest physical therapy, antibiotics, normothermia or mild hypothermia, sedation, paralysis, and increased oxygen concentration). Indications for ECMO by the NIH are as follows: Pao_2 less than 50 mm Hg for more than 2 hours with FIO_2 of 1.0 and conventional PEEP; and a Pao_2 less than 50 mm Hg for more than 12 hours with FIO_2 of more than 0.6 and conventional PEEP. Active bleeding is the only absolute contraindication to use of the artificial lung. The three routes for ECMO are as follows: venovenous perfusion from the inferior vena cava by way of the femoral vein to the oxygenator and then to the superior vena cava; venoarterial perfusion from the femoral vein to the oxygenator and then to the femoral artery; and venovenous arterial perfusion from the femoral vein to the oxygenator and then to both the internal jugular vein and the femoral artery.

A collaborative study on ECMO has been completed under the auspices of the National Heart, Lung, and Blood Institute of the NIH. The results of this controlled study are as follows:

- Compared with the control group of conventional respiratory therapy, ECMO did not improve mortality (90%), and the predominant cause of death was still progressive respiratory failure.
- ECMO did not affect the progress of disease (or lung pathology in those patients who died) any differently from conventional respiratory therapy.
- Although ECMO is an effective means of short-term life support, its clinical application for the treatment of ARDS is not appropriate or economically justified.

However, the recent randomized controlled study of 180 patients in the United Kingdom (CESAR trial) that referred patients with respiratory failure to a specialized facility with an ECMO-based management protocol demonstrated an overall improvement in survival (63% vs. 47%) with an acceptable economic cost.

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Fisher JC, Stolar CJ, Cowles RA. Evaluating cannulation strategies used during second courses of extracorporeal membrane oxygenation in a large cohort of pediatric patients. *J Pediatr Surg*. 2009;44(1):94–99.

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Taghavi S, Ankersmit HJ, Wieselthaler G, et al. Extracorporeal membrane oxygenation for graft failure after heart transplantation: recent Vienna experience. *J Thorac Cardiovasc Surg*. 2001;122(4):819–820.

D.13. What is high-frequency positive pressure ventilation (HFPPV)? What are its characteristics?

HFV was originally used as a technique to provide adequate oxygenation and alveolar ventilation for rigid bronchoscopy and laryngeal surgery. Since that time, the literature is replete with clinical applications of HFV. The major characteristics of the ventilatory pattern of volume-controlled HFPPV are as follows:

- A ventilatory frequency of approximately 60 to 100 per minute and an inspiration/expiration ratio of less than 0.3
- Smaller tidal volumes and therefore lower maximum and mean airway and transpulmonary pressures, yet a higher FRC than in conventional PPV
- Positive intratracheal and negative intrapleural pressures throughout the ventilatory cycle
- Less circulatory interference than in IPPV and/or continuous positive pressure ventilation
- Reflex suppression of spontaneous respiratory rhythmicity during normoventilation
- Decelerating inspiratory flow without an end-inspiratory plateau
- More efficient pulmonary gas distribution than in IPPV and/or continuous positive pressure ventilation

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1061–1062.

Sjostrand U. High frequency positive-pressure ventilation (HFPPV): a review. *Crit Care Med*. 1980;8:345–364.

D.14. What are the frequencies used in high-frequency ventilation (HFV)? How are they classified?

HFV is a generic term encompassing any form of mechanical ventilation operating at a frequency at least four times higher than the natural breathing frequency of the subject being ventilated.

Smith categorized HFV into three groups:

- HFPPV, 60 to 110 per minute
- High-frequency jet ventilation, 110 to 400 per minute
- High-frequency oscillatory ventilation (HFOV), 400 to 2,400 per minute

Froese summarized HFV into five groups as shown in Figure 3.6.

Sjostrand, in Sweden, first introduced HFPPV. It was administered with a very low compliant ventilator with high gas flow rates. This produces a flow profile with rapid upstroke to a high peak flow rate, followed by a passive expiration. Because it is a closed circuit, there was no entrainment of additional gas during inspiration.

High-frequency jet ventilation delivers a small tidal volume at a high flow rate by means of a narrow orifice at an adjustable drive pressure, rate, and inspiratory time or I/E ratio. Gas is regulated by a solenoid or fluidic mechanism. Because jet flow is

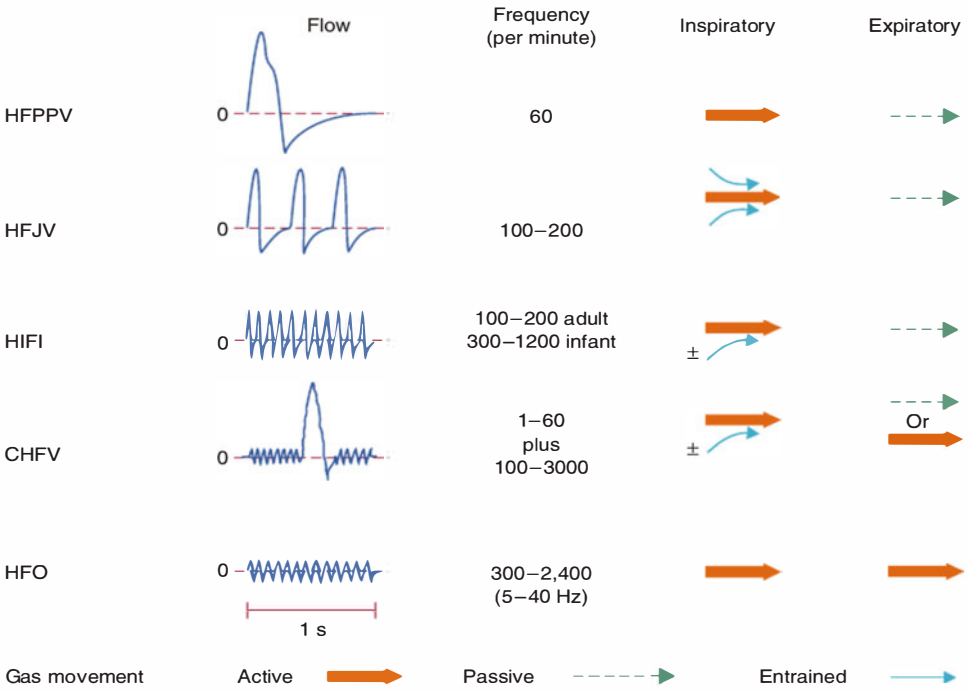

Figure 3.6 Summary of features of several commonly encountered high-frequency modalities. See text for details. CHFV, combined high-frequency ventilation; HFJV, high-frequency jet ventilation; HFOV, high-frequency oscillatory ventilation; HFPPV, high-frequency positive pressure ventilation; HIFI, high fidelity. (From Froese AB. High-frequency ventilation; uses and abuses. *ASA Refresher Courses in Anesthesiology.* Park Ridge, IL: American Society of Anesthesiologists, 1986:127–138, with permission.)

delivered to a small-lumen tube, entrainment occurs due to subatmospheric pressure created at the distal end of a cannula. Exhalation occurs around the tube or through another lumen and is passive. Frequencies are commonly 100 to 200 per minute, occasionally up to 400 per minute.

High-frequency flow interrupters are closely related to jet ventilators. Gas from a high-pressure source is "chopped" into pulses by a rotating ball valve and directed into the lung. The frequencies are usually 100 to 200 per minute in adults and 300 to 1,200 per minute in infants.

CHFV means combined high-frequency ventilation. Combined approaches usually superimpose some form of HFV onto backup conventional mechanical ventilation. The reported combinations vary considerably, with the slow component ranging from 1 to 60 per minute, and the fast component being delivered at 100 to 3,000 per minute.

HFOV is delivered by an oscillator-type ventilator consisting of a rotary-driven piston to produce to-and-fro movement of gas within the airway. Unlike all the other modalities, during HFOV the ventilator actively drives both inspiratory and expiratory flows.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1061–1062.

Butler WJ, Bohn DJ, Bryan AC, et al. Ventilation by high frequency oscillation in humans. *Anesth Analg*. 1980;59:577–584.

Carlon GC, Kahn RC, Howland WS, et al. Clinical experience with high frequency jet ventilation. *Crit Care Med*. 1981;9:1–6.

El-Baz N, Faber LP, Doolas A. Combined high frequency ventilation for management of terminal respiratory failure: a new technique. *Anesth Analg*. 1983;62:39–49.

Froese AB. High frequency ventilation: uses and abuses. In: Barash PG, ed. *ASA Refresher Courses in Anesthesiology*. Park Ridge, IL: American Society of Anesthesiologists; 1986:127–138.

Smith RB. Ventilation at high respiratory frequencies. *Anaesthesia*. 1983;37:1011.

D.15. What are the indications and precautions for HFV?

The indications for HFV include the following:

- Respiratory failure with bronchopleural fistula, tracheoesophageal or bronchoesophageal fistula, barotrauma, pulmonary fibrosis, and pulmonary hemorrhage, because of low airway pressure with HFV.
- Anesthesia for special procedures, such as bronchoscopy, laryngoscopy, tracheal reconstruction over a T-tube, and laser resection of a bronchial lesion, because HFV uses a small cannula for ventilation, leaving adequate room for surgeons to operate.
- Anesthesia for open thoracic surgery because of a moderately expanded lung and minimal respiratory movement with HFV.
- Improving oxygenation in adult and infant respiratory distress syndrome when hypoxemia persists in spite of maximal conventional ventilatory support.
- Enhancement of CO_2 elimination when conventional mechanical ventilation has been unable to support adequate CO_2 elimination despite multiple adjustments of ventilator settings in situations such as persistent fetal circulation in the neonate. HFV could prove advantageous in achieving a respiratory alkalosis by hyperventilation at low peak and mean airway pressures.

The precautions with HFV include the following:

- HFV must never be used in a situation in which expiratory outflow of gas from the lung is impeded. Under such circumstances, lethal barotrauma can occur.

- HFV should never be used with inadequate humidification, because serious tracheal injury may occur.
- HFV system pressure should be accurately and appropriately sampled and monitored in order to drive an automatic shutoff mechanism so gas entry into the lungs can be terminated immediately if an overpressure situation occurs.
- HFV should never be used without adequate training.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1061–1062.

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Carlon GC, Howland WS, Ray C, et al. High frequency jet ventilation. A prospective randomized evaluation. *Chest*. 1983;84:551–559.

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D.16. What is nitric oxide (NO)? What is the role of inhaled NO in the treatment of ARDS?

In 1987, endothelium-derived relaxing factor was identified as NO. NO produced by the endothelium diffuses into vascular smooth muscle where NO activates soluble guanylate cyclase. The subsequent increase in intracellular cyclic guanosine monophosphate causes smooth muscle vasodilation. Endothelium-independent nitrovasodilators such as nitroglycerin and nitroprusside also act through guanylate cyclase activation to directly release NO.

Inhaled NO is a selective pulmonary vasodilator. NO is not effective during systemic administration because it is rapidly inactivated by hemoglobin. Therefore, inhaled NO may diffuse from the alveoli to pulmonary vascular smooth muscle and produce pulmonary vasodilation without systemic vasodilation because any NO that diffuses into blood will be inactivated by hemoglobin. Inhaled NO has been shown to be effective in treating primary pulmonary hypertension, as well as decreasing pulmonary hypertension and improving oxygenation after mitral valve replacement and in the newborn with persistent pulmonary hypertension.

Pulmonary hypertension and hypoxemia universally occur in ARDS. Pulmonary hypertension in ARDS may be due to active vasoconstriction from local alveolar hypoxic pulmonary vasoconstriction and other vasoconstrictor mediators. Hypoxemia in ARDS is due to ventilation/perfusion mismatch, intrapulmonary shunting, or anatomic shunting. Intravenous pulmonary vasodilator therapy with agents such as nitroglycerin, nitroprusside, prostaglandin E, prostacyclin, adenosine, and nifedipine produces small reduction in pulmonary artery pressure but large reduction in systemic blood pressure and arterial oxygenation. The adverse effect on oxygenation is primarily due to reversal of hypoxic pulmonary vasoconstriction. On the contrary, inhaled NO may decrease pulmonary hypertension and improve oxygenation in patients with ARDS because inhaled NO may be distributed according to ventilation so the associated vasodilation increases blood flow to well-ventilated alveoli.

Rossaint et al. published the first major report of the use of inhaled NO in patients with ARDS. They found that inhaled NO (5 to 20 parts per million [ppm]) effectively decreased pulmonary hypertension and improved oxygenation. In a subsequent study, they showed that inhaled concentrations of only 60 to 250 parts per billion could increase Pao_2 by 30%. These concentrations had little or no effect on pulmonary artery pressure. The other major study by Bigatello et al. demonstrated that inhaled NO produced dose-related decreases in pulmonary artery pressure with 50% of the maximal effect occurring at 5 ppm. Inhaled NO also increased oxygenation, but dose-response effects could not be demonstrated.

Inhaled NO has been effective on ARDS in combination with other therapies. The combination of inhaled NO (5 to 10 ppm) and almitrine bismesylate, a potentiator of hypoxic pulmonary vasoconstriction, had additive effects on improving oxygenation in ARDS and simultaneously decreased pulmonary hypertension. Dcering et al. studied intravenous phenylephrine, 50 to 200 μg per minute, titrated to a 20% increase in mean arterial pressure; inhaled NO, 40 ppm; and the combination of phenylephrine and NO. They found that phenylephrine alone can improve Pao_2 in patients with ARDS. In phenylephrine-responsive patients, phenylephrine augments the improvement in Pao_2 seen with inhaled NO. These results may reflect selective enhancement of hypoxic pulmonary vasoconstriction by phenylephrine, which complements selective vasodilation by inhaled NO.

However, an important unsolved issue is the potential pulmonary toxicity of inhaled NO. Toxicity may be due to NO itself, or to its reactive metabolite, NO_2. NO can combine with superoxide anion to produce peroxynitrite anion, which is a powerful oxidizing agent. The effects of NO and NO_2 on repair versus fibrosis in injured lung and on pulmonary host defenses are unknown. Therefore, the effects of inhaled NO on outcome in patients with ARDS are not predictable.

Overall, a recent Cochrane analysis found a transient improvement in oxygenation in patients with ARDS receiving NO but was unable to demonstrate a mortality benefit. Additionally, NO therapy may increase the risk of renal impairment in adult patients with ARDS.

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E. Weaning from Ventilatory Support

The patient's condition improved after respiratory support with 20 cm H_2O PEEP. Arterial blood gas analysis showed the following: pH, 7.45; $Paco_2$, 35 mm Hg; Pao_2, 150 mm Hg; Fio_2, 0.75.

E.1. What would you do now?

The arterial blood gas analysis suggests that the oxygenation has improved markedly; nevertheless, there continues to be significant intrapulmonary shunting and the level of PEEP remains high. Before making any drastic changes, it is important to examine the patient thoroughly to determine that in fact the lung injury is resolving and that there is no evidence of infection, systemic inflammatory involvement, and metabolic derangements. The most appropriate ventilatory change is to lower the F_{IO_2} to less than 0.5 or 0.6. This should be well tolerated. Next, the PEEP should be lowered gradually. The suggested criteria to lower PEEP level are a stable, nonseptic patient; P_{aO_2}/F_{IO_2} more than 200 mm Hg; effective compliance, more than 25 mL per cm H_2O; $P_{AO_2}-P_{aO_2}$, less than 200 mm Hg at F_{IO_2} 0.5. PEEP should not be decreased by more than 5 cm H_2O during a trial. At least 6 hours should elapse before undertaking a further attempt at lowering the PEEP level.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:125–126.

Tobin MJ. 1999 Donald F Egan scientific lecture: weaning from mechanical ventilation: what have we learned? *Respir Care*. 2000;45:417–431.

E.2. The patient continued to improve. When would you consider weaning the patient from the respirator? Discuss the criteria for weaning.

The criteria for discontinuance of mechanical ventilation are essentially the converse of the criteria for the institution of mechanical support and are as follows:

- Clear consciousness with adequate gag and cough reflex
- Cardiovascular stability
- Stable metabolic state without hypothermia, hyperpyrexia, metabolic acidosis, or alkalosis
- Adequate pulmonary function

Mechanics

- A vital capacity of more than 10 mL per kg or more than twice the normal tidal volume
- Rapid shallow breathing index (respiratory frequency/tidal volume) of less than 105 breaths/min/L
- A maximum inspiratory force of at least −20 to −30 cm H_2O

Oxygenation

- P_{aO_2} more than 80 mm Hg with F_{IO_2} at 0.4
- $P_{AO_2}-P_{aO_2}$ less than 300 mm Hg with F_{IO_2} at 1.0
- Q_S/Q_T less than 15%

Ventilation

- P_{aCO_2} less than 45 mm Hg
- V_D/V_T less than 0.6

Lumb AB. *Nunn's Applied Respiratory Physiology*. 6th ed. Philadelphia: Elsevier Butterworth-Heinemann; 2005:430–431.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone Elsevier; 2010:2879–2897.

E.3. Describe weaning by synchronized intermittent mandatory ventilation (SIMV), pressure support, continuous positive airway pressure (CPAP), and T-piece.

Mechanical ventilatory assistance is often an obligatory step during management of critically ill patients; however, complete withdrawal from this support represents a significant clinical problem in approximately 25% of intubated patients. Frequently employed weaning techniques have included PSV, T-piece, CPAP, and SIMV. Several studies have compared these various weaning approaches, but the results have been conflicting. Brochard et al. compared weaning by PSV, T-piece, and SIMV and found weaning by PSV to be superior to weaning by T-piece and by SIMV. In contrast, in a large multicenter trial of nonsurgical patients with diverse medical problems, Esteban et al. demonstrated that the duration of weaning by T-piece once a day was significantly less than weaning by PSV, which in turn was less than weaning by SIMV. Kollef et al. showed that a protocol-guided weaning by nurses and respiratory therapists was safe and led to extubation more rapidly than physician-directed weaning. Therefore, in addition to differences in study design, weaning modalities, and weaning techniques, there are selection and physician biases that interfere with the process of weaning. Although employment of protocol-driven weaning may control for physician bias, it is also data driven, time consuming, and costly.

Conventional T-piece technique

When the patient meets the criteria for weaning, a T-piece adapter and heated nebulizer are connected to the patient's endotracheal tube. The patient should be in a semisitting or sitting position. The inspired oxygen concentration is set at a level 5% to 10% higher than what the patient was receiving during mechanical ventilation. The vital signs and cardiac rhythm are monitored carefully every 5 to 10 minutes. Arterial blood gases are determined 15 minutes after weaning is begun and then every hour. The patient who tolerates the T-piece very well is extubated after 2 to 4 hours. Oxygen is then administered through a face mask with a heated nebulizer, at the same inspired oxygen concentration as during the T-piece trial.

The high success associated with T-piece weaning is related primarily to the fact that the clinician biases are removed from the process. In other words, the patient becomes the sole controller of his or her weaning and readiness for extubation. No guessing is involved. One is either ready or not for weaning, and the best way to determine this is to apply no support. The weaning process is very difficult because the patient's need varies on a breath-by-breath basis, such that the clinician is incapable of predicting such changes. The common error is to be too conservative, thereby prolonging the weaning process.

SIMV technique

Weaning is accomplished by a gradual decrease in the SIMV rate that the ventilator delivers, allowing the patient slowly to take over spontaneous ventilation. This system allows the patient to breathe spontaneously between the preset mechanical ventilation. This system ensures intermittent hyperinflation of the lung.

Weaning by SIMV is the least effective approach in terms of weaning time. It promotes dependence on the ventilator and can be "confusing" to the respiratory center. The delivery of the mechanical breath must coincide with the central inspiratory time. The same rule applies during exhalation. Prolonging the mechanical breath will overlap with the neural start of exhalation; that is, although the neural input is telling the patient to exhale, the ventilator continues to inflate the lungs. This is frequently seen in patients with COPD whose airway flow changes more slowly and the expiratory muscle becomes active during ventilator-induced inflation. A mismatch can also occur if the patient's inspiratory drive occurs before exhalation is complete, leading to "breath stacking."

Another important aspect of synchronization during PPV is the flow rate that changes on an intrabreath and an interbreath basis. Frequently, patients will show signs of "air hunger" and tachypnea if the inspiratory flow rate is inadequate. In most

ventilators, the flow rate is set at 60 L per minute. Too much flow is also problematic. Occasionally, the flow rate is increased to lower the inspiratory time while increasing the exhalation time. Unfortunately, the patient may respond adversely by becoming tachypneic, resulting in shortened expiratory times, which then potentiates dynamic hyperinflation (intrinsic PEEP). Several studies have shown a flow-related inspiratory termination reflex. Activating such reflexes can result in curtailing the neural inspiration producing shallow inspiratory efforts. Overall, the consequences of poor synchronization include increase in work of breathing, anxiety, patient discomfort, ineffective ventilation, and increased morbidity and mortality.

Pressure-support weaning

Pressure-support weaning can be combined with IMV and with CPAP weaning. Its proposed advantages include reducing the work of breathing, improving synchronization between the patient and the ventilator, reducing inspiratory pressures, and facilitating weaning. While on IMV, once the patient has been weaned to a minimum rate (i.e., IMV of 4 to 6 breaths per minute), the level of pressure support is gradually reduced (2 to 3 cm H_2O at a time). In some cases, this level of change is performed only once a day, whereas in other cases, the changes may be made several times a day. When the pressure-support level is at a minimum (<8 cm H_2O), weaning parameters are obtained in preparation for complete withdrawal from the mechanical ventilation. Attention to the pressure–volume and flow waveforms, which are available in most

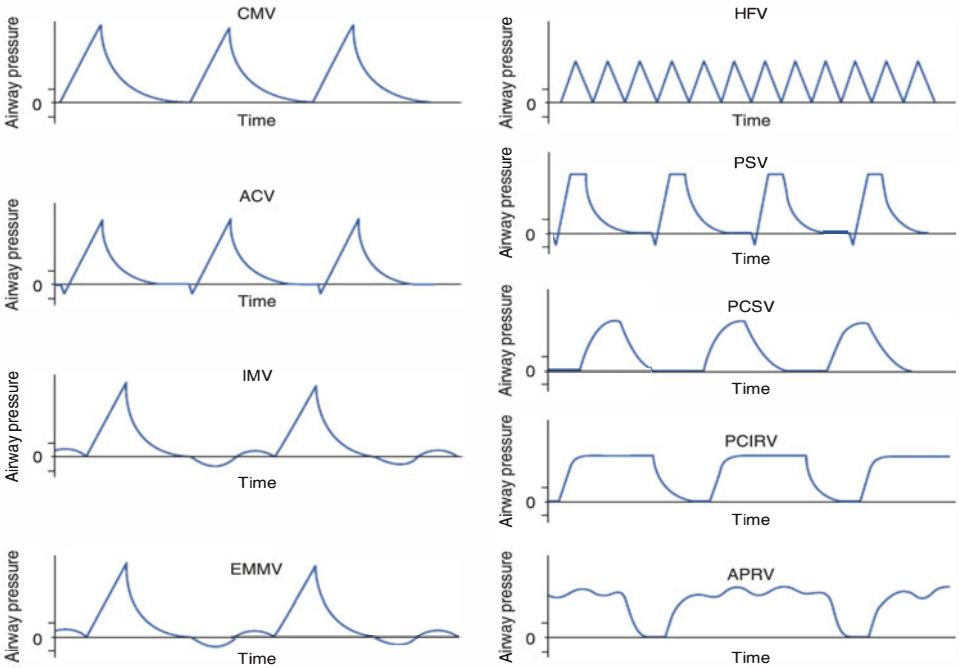

Figure 3.7 Airway pressure waveforms. ACV, assist/control ventilation; APRV, airway pressure-release ventilation; CMV, controlled mechanical ventilation; EMMV, extended mandatory minute ventilation; HFV, high-frequency ventilation; IMV, intermittent mandatory ventilation; PC–IRV, pressure-controlled inverse-ratio ventilation; PCV, pressure-controlled ventilation; PSV, pressure-support ventilation. (From Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2001:1470, with permission.)

mechanical ventilators, can facilitate the weaning process and help determine other important aspects of respiratory mechanics (Fig. 3.7).

As with IMV, the inherent problem with pressure-support weaning is the clinical biases that exist. Once again, the technology and the knowledge that allow for minute-to-minute assessment and adjustment of the dynamic environment of the patient's physiology needs are lacking. Consequently, we make predictions about the level of support the patient needs and await clinical and laboratory signs of problems or success.

Noninvasive ventilation to facilitate weaning

Noninvasive positive pressure ventilation (NIPPV) allows for patients to receive ventilatory support to decrease work of breathing, augment tidal volumes, improve gas exhange while preserving their ability to speak and cough. Additionally, NIPPV can reduce the risk of ventilator associated pneumonia. In a recent systematic review by Burns and colleagues, that examined the use of NIPPV to facilitate liberation from mechanical ventilation, the data suggested a mortality benefit and decrease in the incidence of ventilator associated pneumonia, especially in those with COPD.

Overall, difficulties with weaning can be ascribed in part to the heterogeneity of underlying pulmonary diseases and to inconsistencies in clinical practice. Data-driven approaches to weaning are often are nonpredictive of outcome and may fail to provide clinicians with signs of impending respiratory muscle fatigue. The patient's respiratory demand can vary considerably, requiring appropriate and timely ventilatory adjustments.

Brochard L, Rauss A, Benito S, et al. Comparison of three methods of gradual withdrawing from ventilatory support during weaning from mechanical ventilation. *Am J Respir Crit Care Med.* 1994;150:896–903.

Burns KE, Adhikari NK, et al. Use of non-invasive ventilation to wean critically ill adults off of mechanical ventilation: meta-analysis and systematic review. *BMJ.* 2009;338:1574.

Esteban A, Frutos F, Tobin MJ, et al. A comparison of four methods of weaning patients from mechanical ventilation. *N Engl J Med.* 1995;332:345–350.

Franchi F, Palomba C, Mastrocinque E, et al. Non-invasive mechanical ventilation in the weaning process: contiuous hemodynamic monitoring. *Crit Care*. 2010;14:241.

Kollef MH, Shapiro SD, Silver P, et al. A randomized, controlled trial of protocol-directed versus physician-directed weaning from mechanical ventilation. *Crit Care Med.* 1997;25:567–574.

CHAPTER 4

Lung Transplantation

Nanhi R. Mitter and Charles W. Hogue, Jr.

A 52-YEAR-OLD WOMAN

with progressively worsening dyspnea on exertion, limitation of daily activity despite supplemental oxygen, and radiographic and spirometric evidence of severe obstructive pulmonary disease was scheduled for bilateral sequential lung transplantation. History was remarkable for 30 pack-years of smoking (although none for 10 years), mild hypertension (145/86 mm Hg), normal left ventricular ejection fraction, and osteoarthritis.

A. Medical Disease and Differential Diagnosis

1. What were the expected manifestations of severe obstructive pulmonary disease in this patient, and why is she a transplant candidate?
2. What other end-stage lung diseases can also be treated with transplantation?
3. How many lung transplantations have been performed?
4. What are the selection criteria for recipients?
5. How is the decision made to transplant one or both lungs, and does this influence preoperative management?
6. How does a single-lung transplantation differ technically from a double-lung transplantation?

B. Preoperative Evaluation and Preparation

1. What preoperative evaluation is desirable?
2. How would you premedicate this patient?
3. What vascular access is required?
4. Is preoperative epidural catheter placement advantageous?

C. Intraoperative Management

1. What special equipment is necessary?
2. How would you monitor this patient?

3. How would you induce anesthesia in this patient?
4. How would you ventilate this patient? What kind of endotracheal tube would you use?
5. How does the physiology of single-lung ventilation influence the procedure?
6. Should volatile anesthetics be avoided during single-lung ventilation?
7. At what specific points in the procedure are problems anticipated?
8. What problems are associated with the lateral position?
9. How does single-lung ventilation affect cardiopulmonary function? What are the problems of single-lung ventilation in this patient? How would you treat them?
10. How would you deal with problems related to clamping of the pulmonary artery?
11. What hemodynamic alterations would you expect during graft implantation and reperfusion? How would you correct them?
12. When is cardiopulmonary bypass (CPB) necessary for lung transplantation?
13. Should fluid administration be restricted, and are blood products commonly required?
14. Would you extubate the patient upon conclusion of the procedure?

D. Postoperative Management

1. What are the major complications after lung transplantation?
2. How is postoperative ventilation managed, and for how long is it required?
3. What special precautions should be taken when a lung transplant recipient requires general anesthesia for subsequent nonpulmonary surgery?
4. What are the long-term outcomes of lung transplantation?
5. Are there surgical alternatives to lung transplantation?

A. Medical Disease and Differential Diagnosis

A.1. What were the expected manifestations of severe obstructive pulmonary disease in this patient, and why is she a transplant candidate?

This patient suffered from increased airway resistance, reduced expiratory flow rates, and high residual lung volumes. When expiratory airway obstruction and lung hyperinflation become so severe that the chest cannot physically expand to accommodate a normal tidal volume, restrictive physiology becomes superimposed on obstructive disease. This condition is usually refractory to medical management and substantially limits daily activity. This patient's age and lack of other major systemic illness allowed her to be considered a transplant candidate.

Chronic obstructive pulmonary disease (COPD) (36%), idiopathic pulmonary fibrosis (21%), emphysema secondary to α_1-antitrypsin deficiency (7%), and cystic fibrosis (16%) are the most common obstructive disorders in adults undergoing lung transplantation. At one time, concerns about mediastinal displacement and profound ventilation–perfusion mismatch secondary to hyperinflation of the remaining native lung prevented surgeons from attempting single-lung transplantation for emphysema. However, clinical experience has demonstrated that many patients with emphysema can be successfully treated by single-lung transplantation. Because of the severe shortage of organs for transplant, single-lung procedures have been advocated as a means to increase the number of recipients. However, with 5-year survival rates after single-lung transplantation approaching only 50% and increasing experience suggesting that bilateral lung transplantation for COPD is associated with improved functional outcomes and improved long-term survival, bilateral lung transplantation emerged as a formidable (alternative)

approach to treat this patient population. The improved survival with bilateral lung transplantation may possibly be due to the later development of bronchiolitis obliterans syndrome, as well as a trend for higher quality of life score compared with single-lung transplantation. Nevertheless, although transplantation may improve quality of life for patients with severe COPD, the decision for single-lung or bilateral lung transplantation remains controversial and is based on the individual situation, taking into account regional organ allocation policies, individual center experience, and organ availability.

Christie JS, Edwards LB, Aurora P, et al. Registry of the international society for heart and lung transplantation: twenty-sixth official adult lung and heart-lung transplantation report—2009. *J Heart Lung Transplant.* 2009;28:1031–1049.

Meyer DM, Bennet LE, Novick RJ, et al. Single vs bilateral sequential lung transplantation for end-stage emphysema: influence of recipient age and secondary end-points. *J Heart Lung Transplant.* 2001;20:935–941.

Sundaresan RS, Shiraishi Y, Trulock EP, et al. Single or bilateral lung transplantation for emphysema? *J Thorac Cardiovasc Surg.* 1996;112:1485.

Todd JL, Palmer SM. Lung transplantation in advanced COPD: is it worth it? *Semin Respir Crit Care Med.* 2010;31:365–372.

A.2. What other end-stage lung diseases can also be treated with transplantation?

The first successful (i.e., the patient left the hospital) single-lung transplantations were performed in 1983 for idiopathic pulmonary fibrosis. Since that time, the procedure has been applied to patients suffering from various end-stage pulmonary diseases (Table 4.1). In general, the underlying disease processes produce lung dysfunction that can be broadly characterized as obstructive, restrictive, infectious (e.g., cystic fibrosis and bronchiectasis), or vascular. As of 2008, most single-lung transplantations were performed for obstructive lung disease, followed by idiopathic pulmonary fibrosis. The most common indications for bilateral lung transplantation are cystic fibrosis and obstructive lung disease.

Reflecting a loss of lung parenchymal elasticity and compliance, end-stage restrictive disease is characterized by profoundly reduced lung volumes and diffusing capacity but relative preservation of ventilatory flow rates. Comparison of flow–volume loops representing obstructive and restrictive diseases is shown in Figure

Table 4.1 Lung Transplants Categorized by Disease

END-STAGE LUNG DISEASE	SINGLE-LUNG TRANSPLANT (% OF TOTAL)	BILATERAL/DOUBLE-LUNG TRANSPLANT (% OF TOTAL)
Cystic fibrosis	1.9	26.6
Retransplant	2.6	1.7
Idiopathic pulmonary arterial hypertension	0.7	5.4
α_1-Antitrypsin deficiency	6.5	7.6
Sarcoidosis	2.1	2.9
Idiopathic pulmonary fibrosis	29.1	14.5
Emphysema/chronic obstructive lung disease	49	25
Miscellaneous	5.2	6.6

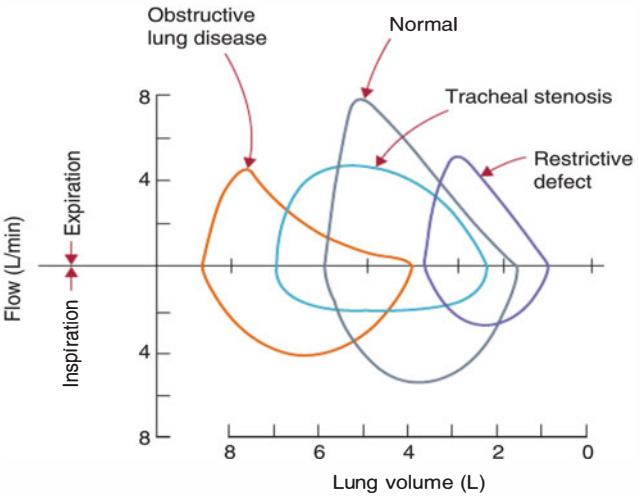

Figure 4.1 Representative tracings of flow–volume loops from a healthy individual, a patient with parenchymal obstructive disease, a patient with tracheal stenosis, and a patient with restrictive disease from parenchymal fibrosis. (Adapted from Goudsouzian N, Karamanian A. *Physiology for the Anesthesiologist.* 2nd ed. Norwalk, CT: Appleton-Century-Crofts; 1984:213.)

4.1. The underlying disease process also tends to obliterate pulmonary microvasculature, thereby chronically increasing vascular resistance, producing pulmonary hypertension, and predisposing to cor pulmonale. Most patients with restrictive disease are good candidates for a single-lung transplantation because the stiff, vasoconstricted native lung will receive relatively little ventilation and perfusion and can, therefore, usually be left without compromising the transplanted lung.

Infectious lung disease such as cystic fibrosis is the most frequent indication for lung transplantation in patients younger than 18 years. Characterized by chronic infection and the production of copious purulent secretions, patients with cystic fibrosis primarily exhibit functional abnormalities that are obstructive with increased airway reactivity. Under most circumstances, residual volumes and functional residual capacity are increased, and bronchodilators have little effect on expiratory flow rates. Because of potential infectious cross-contamination of the transplanted lung, chronic infectious disease represents a contraindication to single-lung transplantation. Nevertheless, single-lung transplantation with contralateral pneumonectomy has been performed and suggested as an alternative solution.

Pulmonary vascular disease with severe pulmonary hypertension and right ventricular dysfunction has also emerged as an indication for transplantation. Pathologically, severe pulmonary artery hypertension can result from idiopathic proximal vascular processes such as persistent pulmonary hypertension (PPH) or secondary to chronically increased pulmonary blood flow (e.g., left-to-right intracardiac shunt, leading to Eisenmenger syndrome) or pulmonary venous hypertension. Pulmonary hypertension may precipitate chronic hypoxemia if it is associated with an intracardiac defect that allows for development of a right-to-left shunt. Improved medical therapy for PPH, particularly with continuous long-term intravenous prostacyclin infusions or sildenafil, has affected the number of patients undergoing lung transplantation for this disease at some centers.

Controversy exists with respect to choice of single-lung versus bilateral lung transplantation for patients with idiopathic pulmonary arterial hypertension (IPAH).

Because a native lung can usually be left intact without compromising a transplanted lung (which will receive most of the blood flow), some patients with pulmonary vascular disease may be reasonable candidates for single-lung transplantation, with concurrent repair of any cardiac anomalies. Early reports indicated poorer functional recovery and higher mortality after single-lung versus bilateral lung transplantation for PPH. Some reports suggest the earlier manifestation of bronchiolitis obliterans syndrome in patients after single-lung versus bilateral lung transplantation, and although survival curves diverge 3 years after transplantation, controversy remains as to whether procedure type is the main cause. Some centers have adopted bilateral lung transplantation as the mainstay of treatment for patients presenting with IPAH.

Christie JS, Edwards LB, Aurora P, et al. The registry of the international society for heart and lung transplantation: twenty-sixth official adult lung and heart-lung transplantation report—2009. *J Heart Lung Transplant.* 2009;28:1031–1049.

Gammie JS, Keenan RJ, Pham SM, et al. Single- versus double-lung transplantation for pulmonary hypertension. *J Thorac Cardiovasc Surg.* 1998;115:397–402.

Mendeloff EN, Meyers BF, Sundt TM, et al. Lung transplantation for pulmonary vascular disease. *Ann Thorac Surg.* 2002;73:209–219.

Pasque MK, Kaiser LR, Dresler CM, et al. Single lung transplantation for pulmonary hypertension: technical aspects and immediate hemodynamic results. *J Thorac Cardiovasc Surg.* 1992;130:475–482.

Shennib H, Massard G, Gauthier R, et al. Single lung transplantation for cystic fibrosis: is it an option? *J Heart Lung Transplant.* 1993;12:288–293.

A.3. How many lung transplantations have been performed?

Although the first human lung allograft was performed in 1963, transplantation of one or both lungs did not emerge as a viable therapeutic option for patients with end-stage lung disease until the 1980s. The ultimate emergence of this procedure can be largely attributed to advances in the prevention and treatment of airway complications, infections, and rejection. Since initiation of an international registry for lung transplantation in the mid-1980s, the number of procedures reported yearly rose sharply, until beginning to slow in 1993. To date, the highest yearly total was 2708 in 2008. Despite this volume, the number of patients awaiting lung transplantation continues to exceed the limited donor supply. As of the 2009 international registry, 29,732 lung transplantations had been reported worldwide.

Christie JS, Edwards LB, Aurora P, et al. The registry of the international society for heart and lung transplantation: twenty-sixth official adult lung and heart-lung transplantation report—2009. *J Heart Lung Transplant.* 2009;28:1031–1049.

Hardy JD, Webb WR, Dalton ML, et al. Lung homotransplantation in man. *JAMA.* 1963;186:1065–1074.

Trulock EP. Lung transplantation. *Am J Respir Crit Care Med.* 1997;155:789–818.

A.4. What are the selection criteria for recipients?

In general, patients with severe end-stage lung disease are considered candidates for transplantation when their life expectancy is less than 2 to 3 years, they have minimal disease of other organ systems, and they are mentally and psychologically capable of following strict regimens for rehabilitation and immunosuppressive therapy. Specific criteria, including age, depend on the type of lung disease and whether the planned procedure is single-lung or bilateral lung transplantation. Recent data reveal that the

age of lung transplant recipients is increasing, with approximately 35% now 60 years of age and above compared to 15% in 1998. The average age of the recipient is 35.5 years. In contrast to criteria formulated when lung transplantation was in its infancy, concomitant steroid therapy, previous intrathoracic surgery, mechanical ventilation, and right ventricular failure are no longer considered absolute contraindications.

Bigham M, Dickstein ML, Hogue CW Jr. Cardiac and lung transplantation. In: Estafanous FG, Barash PG, Reves JG, eds. *Cardiac Anesthesia*. Philadelphia: Lippincott Williams & Wilkins; 2001:636.

Christie JS, Edwards LB, Aurora P, et al. The registry of the international society for heart and lung transplantation: twenty-sixth official adult lung and heart-lung transplantation report—2009. *J Heart Lung Transplant.* 2009;28:1031–1049.

Myles PS. Pulmonary transplantation. In: Kaplan JA, Slinger PD, eds. *Thoracic Anesthesia.* Philadelphia: Elsevier Science; 2003:295–314.

A.5. How is the decision made to transplant one or both lungs, and does this influence preoperative management?

Single-lung transplantation is often preferred because of the extreme shortage of donor organs; nevertheless, as experience increases with double-lung transplantation and the improvement in outcomes compared with single-lung transplantation, many centers are performing double-lung transplantation more frequently. The only absolute contraindication to single-lung transplantation is infectious lung disease (e.g., cystic fibrosis and bronchiectasis), with which leaving the native lung could endanger long-term viability of the transplanted lung. As noted earlier, severe emphysema was once thought of as a contraindication to single-lung transplantation because of the probability of mediastinal shift and marked ventilation mismatch between the highly dispensable native lung and the graft. This is only rarely of clinical significance, and it is now accepted that single-lung transplantation can be successfully performed in patients with obstructive disease. Although single-lung transplantation is technically easier and advocated for more difficult recipients, such as those with prior thoracic surgery or coexisting illnesses, functional improvements are often better with bilateral lung transplantation. In addition, the status of the donor lungs further influences the decision of whether to perform a single or bilateral procedure. Finally, transplantation of two lobes from two living related donors for patients with inflammatory disease who are unlikely to survive the wait for a cadaver donor is gaining acceptance. From a practical standpoint, the decision to perform a single-lung or bilateral lung transplantation has little impact on preoperative management because both procedures necessitate the same level of preparation.

Date H, Tanimoto Y, Goto K, et al. A new treatment strategy for advanced idiopathic interstitial pneumonia: living-donor lobar lung transplantation. *Chest.* 2005;128:1364–1370.

Myles PS. Pulmonary transplantation. In: Kaplan JA, Slinger PD, eds. *Thoracic Anesthesia*. Philadelphia: Elsevier Science; 2003:295–314.

Sundaresan RS, Shiraishi Y, Trulock EP, et al. Single or bilateral lung transplantation for emphysema? *J Thorac Cardiovasc Surg.* 1996;112:1485.

A.6. How does a single-lung transplantation differ technically from a double-lung transplantation?

It is extremely important that anesthesiologists be broadly familiar with the surgical methods, because manipulation of the heart and lungs at specific points during

the transplantation can produce marked cardiopulmonary disturbances. Ideally, the anesthesiologist will anticipate these changes and adapt the anesthetic management accordingly. Description of the detailed technical aspects of lung transplantation are readily available.

Single-lung transplantation is usually performed in the lateral decubitus position through a thoracotomy incision, often with the upper leg and pelvis angled to allow groin exposure for potential femoral cannulation and CPB. In contrast, bilateral sequential lung transplantation is usually performed with the patient supine through a "clamshell" incision (bilateral anterior thoracotomies with or without transverse sternotomy). For both single-lung and bilateral lung transplantation, intermittent single-lung ventilation is required during dissection of the native lung to be removed and implantation of the graft. Once stable single-lung ventilation is established, dissection of the lung to be transplanted is initiated with isolation of the pulmonary artery. To assess the cardiopulmonary response to diverting the entire cardiac output through one lung, progressive temporary occlusion of the vessel is first performed manually; if well tolerated, the vessel is then clamped and stapled. After ligation of the pulmonary artery, the pneumonectomy is completed. Implantation of the graft begins with anastomosis of the airway. In the past, the bronchial anastomosis was wrapped with an omental pedicle, mobilized through a small abdominal incision in an effort to improve blood supply to the airway and promote healing. However, the use of a "telescoping" bronchial anastomosis has now largely obviated the need for omental wrapping. The pulmonary artery branch is then attached to the graft, followed by anastomosis of a cuff of the left atrium containing the pulmonary veins. The implanted lung is then partially inflated, air is remove from the left atrial cuff and pulmonary veins, and circulation to the organ restored.

Patients presenting for single-lung transplantation with chronic PPH of primary or secondary etiology often exhibit severe functional compromise of the right ventricle. To avoid additional right ventricular stress, many institutions choose to institute partial normothermic CPB during single-lung transplantation for PPH or in patients with severe pulmonary hypertension and right ventricular dysfunction secondary to restrictive or obstructive disease. Cannulation is typically through the femoral artery and the right atrium unless simultaneous correction of an intracardiac defect is planned. In such patients, conventional aortic and single- or double-stage atrial cannulation are performed. Implantation of the lung is otherwise performed in the same manner as described earlier.

Double-lung transplantation was first described by the Toronto Lung Transplant Group in the mid-1980s as en bloc implantation of both lungs simultaneously. The procedure is performed through a median sternotomy using hypothermic CPB, cardioplegic cardiac arrest, and single tracheal (or double bronchial) anastomosis of the trachea and main pulmonary artery. Although the procedure initially produced encouraging results, considerable limitations related to technical complexity, morbidity, mortality, and application to many patients with end-stage lung disease soon became apparent. Not surprisingly, use of the procedure declined sharply and has now been largely replaced by the bilateral sequential implantation technique, which does not uniformly require hypothermic CPB. Introduced in 1990, bilateral sequential (or bilateral single) lung transplantation has become the surgical procedure of choice when replacement of both lungs is necessary. According to the 2009 International Registry, 69% of the transplants performed were bilateral lung transplantations. As noted earlier, in contrast to single-lung transplantation, bilateral sequential lung transplantation procedures are performed in the supine position. In general, the procedure can be regarded as having two phases. First, the most severely compromised lung (as determined by preoperative ventilation–perfusion lung scanning) is removed during ventilation of the "good" contralateral lung. Implantation is achieved through a bronchial anastomosis as with single-lung

transplantation. The second lung is then removed and transplanted during ventilation of the new lung alone.

Kaiser LR, Cooper JD. Adult lung transplantation. In: Flye MW, ed. *Atlas of Organ Transplantation*. Philadelphia: WB Saunders, 1995:296–312.

Pasque MK, Cooper JD, Kaiser LK, et al. An improved technique for bilateral single lung transplantation: rationale and clinical experience. *Ann Thorac Surg*. 1990;49:785–789.

B. Preoperative Evaluation and Preparation

B.1. What preoperative evaluation is desirable?

At most centers, an extensive physical examination, psychological evaluation, and numerous tests of cardiopulmonary function are performed before acceptance into the transplant program. This facilitates the preanesthetic evaluation that ideally is performed when the patient is first accepted into the transplant program. Familiarity with pulmonary function tests, ventilation–perfusion lung scan results, heart catheterization, echocardiographic data (including evidence of intracardiac shunts), exercise tolerance, oxygen use, and dependence on continuous pulmonary vasodilator infusion (i.e., prostacyclin) are beneficial for formulating an anesthetic plan. Although many of these parameters are regularly reassessed, the interval between evaluation and transplantation necessitates that a careful history and physical examination be performed before the procedure, focusing on signs of pulmonary hypertension and cardiac dysfunction.

Bigham M, Dickstein ML, Hogue CW Jr. Cardiac and lung transplantation. In: Estafanous FG, Barash PG, Reves JG, eds. *Cardiac Anesthesia*. Philadelphia: Lippincott Williams & Wilkins; 2001:636.

Myles PS. Pulmonary transplantation. In: Kaplan JA, Slinger PD, eds. *Thoracic Anesthesia*. Philadelphia: Elsevier Science; 2003:295–314.

B.2. How would you premedicate this patient?

As with all critically ill patients, considerations regarding preoperative sedation are governed primarily by the functional limitations imposed by the underlying disease and the potential consequences of hypercarbia and hypoxemia as a result of the sedation. Consideration must also be given to the possibility that the donor lungs will be deemed unacceptable at final inspection, and therefore the procedure is canceled and the patient discharged from the hospital. When indicated, parenteral sedation is usually chosen because of insufficient time to effectively administer oral anxiolytics. Midazolam alone or with diphenhydramine (potentially protecting the lung against drug-induced histamine release) is often sufficient. Clinically, most patients with end-stage restrictive, obstructive, or infectious lung disease are tachypneic while breathing room air and cannot be aggressively sedated. In contrast, patients with PPH and no intracardiac defect often appear reasonably normal and will benefit from sedation because of the potential for stress-related increases in pulmonary vascular resistance. Alternatively, patients with pulmonary hypertension and significant right-to-left intracardiac shunting (i.e., Eisenmenger physiology) are often cyanotic despite oxygen supplementation and may not tolerate sedation well. In addition, consideration needs be given to immunosuppression protocols and, in appropriate patients, supplemental bronchodilator therapy.

Hartigan PM, Pedoto A. Anesthetic considerations for lung volume reduction surgery and lung transplantation. *Thorac Surg Clin*. 2005;15:143–157.

Myles PS. Pulmonary transplantation. In: Kaplan JA, Slinger PD, eds. *Thoracic Anesthesia*. Philadelphia: Elsevier Science; 2003:295–314.

B.3. What vascular access is required?

Typically, a large-bore intravenous catheter and central venous access for pulmonary artery catheter placement are secured before surgery. In many centers, additional central venous cannulation is performed with a multiple-lumen catheter to provide intraoperative and postoperative venous access. For patients with chronic infectious lung disease or a history of previous intrathoracic procedures, a second large-bore intravenous catheter is often started because of the potential for brisk blood loss during dissection of pulmonary adhesions. Meticulous removal of air from venous infusion lines should be performed, particularly in patents with known or suspected right-to-left shunts. At many institutions, cannulation of a femoral artery, instead of the radial artery, is performed under local anesthesia in the operating room, because radial arterial pressures may become damped during the procedure secondary to positioning of the arms.

Hartigan PM, Pedoto A. Anesthetic considerations for lung volume reduction surgery and lung transplantation. *Thorac Surg Clin*. 2005;15:143–157.

Heerdt PM, Triantafillou AN. Anesthesia for lung transplantation. In: Flye MW, ed. *Atlas of Organ Transplantation*. Philadelphia: WB Saunders; 1995:313–318.

B.4. Is preoperative epidural catheter placement advantageous?

Pain control after lung transplantation can be critical in facilitating patient extubation and rehabilitation. Both lumbar and thoracic epidural catheters have been used for postoperative pain management. At many institutions, catheters are placed immediately before the procedure in most patients, despite the rare possibility of anticoagulation and CPB during the transplantation procedure. This practice is supported by data indicating no adverse sequelae to preoperatively placed epidural catheters, including patients who required emergent heparinization and CPB. Obvious exceptions to this approach are patients who undergo anticoagulation preoperatively or those in whom CPB is planned. Delaying placement of the epidural catheter until the postoperative period may also be a possibility.

Feltracco P, Barbieri S, Milevoj M, et al. Thoracic epidural analgesia in lung transplantation. *Transplant Proc*. 2010;42:1265–1269.

Hartigan PM, Pedoto A. Anesthetic considerations for lung volume reduction surgery and lung transplantation. *Thorac Surg Clin*. 2005;15:143–157.

Myles PS. Pulmonary transplantation. In: Kaplan JA, Slinger PD, eds. *Thoracic Anesthesia*. Philadelphia: Elsevier Science; 2003:295–314.

C. Intraoperative Management

C.1. What special equipment is necessary?

Items necessary for lung transplantation procedures include an anesthesia machine with a ventilator capable of delivering a wide range of inspiratory/expiratory ratios, varying inspired oxygen concentrations, and differing ventilatory modes, as well as efficacy at higher airway pressures. Apparatus to deliver continuous positive airway pressure (CPAP) should be readily available, as should a fiberoptic bronchoscope to

confirm double-lumen tube positioning, provide guided airway suctioning, and inspect anastomosis. Access to transesophageal echocardiography is often beneficial, and a CPB machine should always be immediately available for lung transplantation. Although not specifically approved for this indication, an inhaled nitric oxide (iNO) delivery system is highly desirable during lung transplantation. Other drugs, including vasopressors, inotropes, and selective pulmonary vasodilators, also may be needed in these cases.

C.2. How would you monitor this patient?

Intraoperatively, hemodynamic and respiratory changes are often acute and profound, so extensive monitoring is imperative. In addition to the electrocardiogram, arterial blood pressure, and peripheral arterial oxygen saturation, pulmonary artery catheter placement is routine for lung transplantation at most institutions because of the profound changes in pulmonary and systemic hemodynamics that often occur. During single-lung transplantations, pulmonary artery catheters often migrate to the operative side after the patient has been laterally positioned even when radiographically confirmed to be in the nonoperative lung. Therefore, the surgeon should be reminded to palpate the pulmonary artery and withdraw the catheter if necessary before cross-clamping the vessel. Pulmonary artery catheters capable of measuring mixed venous oxygen saturation have become widely used. Transesophageal echocardiography is often employed during lung transplantation to evaluate right ventricular function, particularly during clamping of the pulmonary artery; to assess for intracardiac shunts; to assess the adequacy of air removal maneuvers; and to evaluate vascular anastomoses.

Bigham M, Dickstein ML, Hogue CW Jr. Cardiac and lung transplantation. In: Estafanous FG, Barash PG, Reves JG, eds. *Cardiac Anesthesia*. Philadelphia: Lippincott Williams & Wilkins; 2001:636.

Miyaji K, Matsubara H, Nakamura K, et al. Equivalence of flow velocities through bilateral pulmonary vein anastomoses in bilateral living-donor lobar lung transplantation. *J Heart Lung Transplant*. 2005;24:860–864.

Myles PS. Pulmonary transplantation. In: Kaplan JA, Slinger PD, eds. *Thoracic Anesthesia*. Philadelphia: Elsevier Science; 2003:295–314.

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C.3. How would you induce anesthesia in this patient?

As with induction of anesthesia in any critically ill patent, multiple techniques have been safely used for patients undergoing lung transplantation. The only general rule is that induction be relatively gradual, because abrupt withdrawal of sympathetic tone in these patients with high sympathetic activity can result in marked cardiovascular compromise, particularly during the transition from spontaneous to mechanical ventilation. For this reason, injecting an epidural catheter with local anesthetic before induction of anesthesia can be problematic. Because effective alveolar ventilation and nitrogen washout are poor in the patient with severe obstructive lung disease and high residual volumes, prolonged (i.e., 15 to 20 minutes) preoxygenation is worthwhile, followed by a rapid-acting induction agent to shorten the excitement stage, expedite airway management, and prevent opiate-induced truncal rigidity. Thiopental, etomidate, propofol, and ketamine have all been used safely, but specific properties

of each drug in the setting of the patient's underlying disease should be considered. Thiopental, for example, may not be desirable for patients with bronchospasm or pulmonary hypertension because of a propensity for histamine release. Alternatively, the sympathomimetic properties of ketamine may preclude use in the presence of pulmonary hypertension, whereas its bronchodilating effects may be beneficial in the setting of bronchospasm. After administration of the hypnotic, fentanyl 10 to 15 μg per kg or sufentanil 1 to 2 μg per kg has been commonly used with either succinylcholine or a nondepolarizing muscle relaxant to complete induction. Benzodiazepines, scopolamine, or volatile anesthetic agents are frequently administered after induction to promote amnesia and in the case of volatile agents to promote bronchodilation.

Bigham M, Dickstein ML, Hogue CW Jr. Cardiac and lung transplantation. In: Estafanous FG, Barash PG, Reves JG, eds. *Cardiac Anesthesia.* Philadelphia: Lippincott Williams & Wilkins, 2001:636.

Hartigan PM, Pedoto A. Anesthetic considerations for lung volume reduction surgery and lung transplantation. *Thorac Surg Clin.* 2005;15:143–157.

C.4. How would you ventilate this patient? What kind of endotracheal tube would you use?

After induction, the trachea is usually intubated with a left endobronchial double-lumen tube for both single-lung and bilateral lung transplantation. Use of a single-lumen endotracheal tube with either an external or an internal bronchial blocking catheter has been described but does not appear to be clearly superior to the left endobronchial tube for most procedures. Furthermore, an endobronchial tube allows for differential lung ventilation if required postoperatively. One exception to this approach has been in patients with cystic fibrosis who exhibit thick, tenacious secretions that are difficult to suction through the small-lumen suction catheters necessary for double-lumen tubes. In these patients, it is often helpful to first place a large single-lumen tube and perform extensive bronchoscopic-directed bronchial lavage and suctioning before placement of the double-lumen tube.

The transition from spontaneous to mechanical ventilation invariably produces hemodynamic alterations resulting from acute changes in intrathoracic pressure and chest wall compliance. With obstructive lung disease, mechanical ventilation magnifies airtrapping, leading to pulmonary tamponade. Varying degrees of this phenomenon should be expected during anesthesia induction. The treatment consists of intermittent apnea with an open ventilator circuit, adjustment of the ventilatory pattern to an inspiratory/expiratory ratio of 1:5 or less with moderate tidal volumes, and administration of bronchodilating drugs. Prompt restoration of blood pressure usually ensues. If hypotension persists, other causes of circulatory compromise must be excluded, including pneumothorax. With restrictive disease, higher inflation pressures and positive end-expiratory pressure (PEEP) are often required. In both patients with obstructive disease and patients with restrictive disease, optimal balance of ventilation with hemodynamic stability often necessitates tolerating a degree of hypercapnia. In patients with pulmonary hypertension, mechanical ventilation usually produces less cardiovascular disturbance if caution is exercised not to increase pulmonary vascular resistance (e.g., from hypoxia, hypercarbia, or lung hyperinflation).

Hartigan PM, Pedoto A. Anesthetic considerations for lung volume reduction surgery and lung transplantation. *Thorac Surg Clin.* 2005;15:143–157.

Triantafillou AN, Heerdt PM, Patterson GA. Lung transplantation. In: Youngberg JA, Lake CA, Roizen MF, et al, eds. *Cardiac, Thoracic and Vascular Anesthesia*. New York: Churchill Livingstone; 2000:703.

C.5. How does the physiology of single-lung ventilation influence the procedure?

In laterally positioned patients, gravity helps redistribute blood away from the nonventilated lung during single-lung ventilation and lessen intrapulmonary shunt. In supine patients, this benefit is obviously lost and single-lung ventilation may not be well tolerated. In general, because of large residual lung volumes that will become filled with a high concentration of oxygen content during the initial stages of the procedure, lung recipients with severe obstructive lung disease may initially maintain oxygenation for the first 10 to 15 minutes of single-lung ventilation. However, rapid arterial desaturation may then occur once a substantial portion of the residual volume is absorbed. Alternatively, patients with restrictive lung disease and a low functional residual capacity may rapidly exhibit both hypoxia and hypercarbia. Multiple steps can be taken to improve oxygenation, including insufflation of oxygen or CPAP to the nonventilated lung, bronchoscopic-guided suctioning of the ventilated lung, careful manipulation of the ventilatory pattern, and PEEP to the ventilated lung. Differential PEEP/CPAP should be done cautiously because increased airway pressure in the ventilated lung can divert blood toward the nonventilated side. In some patients, intermittent ventilation of the operative lung may have to be performed before pneumonectomy. In general, oxygenation improves after clamping of the pulmonary artery supplying the nonventilated lung. For desaturation not responding to the usual maneuvers, tourniquets can be placed around the pulmonary artery by the surgeon as a temporizing step until dissection permits proper stapling of this vessel.

Myles PS. Pulmonary transplantation. In: Kaplan JA, Slinger PD, eds. *Thoracic Anesthesia*. Philadelphia: Elsevier Science; 2003:295–314.

Triantafillou AN, Heerdt PM, Patterson GA. Lung transplantation. In: Youngberg JA, Lake CA, Roizen MF, et al, eds. *Cardiac, Thoracic and Vascular Anesthesia*. New York: Churchill Livingstone; 2000:703.

C.6. Should volatile anesthetics be avoided during single-lung ventilation?

Because of experimental evidence demonstrating inhibition of hypoxic pulmonary vasoconstriction (HPV) by the volatile anesthetic agents, some authors have suggested that these drugs be avoided in the anesthetic management of patients with end-stage lung disease requiring single-lung ventilation. Nevertheless, the true clinical significance of these experimental observations remains somewhat controversial. From a clinical standpoint, commonly used doses of isoflurane (e.g., end-tidal concentrations of $\leq$1.0) have not been empirically associated with worsening of intrapulmonary shunt and hypoxia. Therefore, isoflurane remains widely used in these patients and may actually benefit some lung recipients because of its bronchodilating properties. (See Chapter 2, section C.13.)

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Raffin L, Cherqui MM, Sperandio M, et al. Anesthesia for bilateral lung transplantation without cardiopulmonary bypass: initial experience and review of intraoperative problems. *J Cardiothorac Vasc Anesth*. 1992;6:409–417.

C.7. At what specific points in the procedure are problems anticipated?

Problems can be anticipated at the following points:

- Anesthesia induction
- Lateral positioning
- Single-lung ventilation
- Clamping of the pulmonary artery
- Graft implantation
- Graft reperfusion

C.8. What problems are associated with the lateral position?

Single-lung transplantation is usually performed in the lateral decubitus position, often with the upper leg and pelvis angled to allow groin exposure for potential femoral cannulation and CPB. Not surprisingly, position-related changes in venous return, coupled with compression of the dependent lung by the mediastinum and diaphragm, may promote systemic hypotension and ventilation–perfusion mismatch. Furthermore, pulmonary artery pressure usually tends to rise after lateral positioning, probably because of gravity-induced shifts in pulmonary blood flow distribution, vascular congestion, and increased vascular resistance.

Triantafillou AN, Heerdt PM, Patterson GA. Lung transplantation. In: Youngberg JA, Lake CA, Roizen MF, et al, eds. *Cardiac, Thoracic and Vascular Anesthesia.* New York: Churchill Livingstone; 2000:703.

C.9. How does single-lung ventilation affect cardiopulmonary function? What are the problems of single-lung ventilation in this patient? How would you treat them?

Isolated ventilation of the dependent lung is often accompanied by a marked acute increase in peak inspiratory pressure and a subsequent gradual progressive rise in pulmonary artery pressure. As noted earlier, because of the beneficial effect of gravity on redistributing blood away from the nondependent nonventilated lung, single-lung ventilation is often tolerated better from a respiratory standpoint by patients undergoing single-lung transplantation in the lateral position than those undergoing bilateral lung transplantation in the supine position. Close monitoring of right ventricular performance during conversion to single-lung ventilation is extremely important because of the increase in afterload produced by hypoxic vasoconstriction and redistribution of blood flow. Though unusual, if the right ventricle becomes hypokinetic and distended, and if the ejection fraction decreases, ventilation may have to be altered to minimize pulmonary arterial pressure.

Triantafillou AN, Pasque MK, Huddleston CB, et al. Predictors, frequency, and indications for cardiopulmonary bypass during lung transplantation in adults. *Ann Thorac Surg.* 1994;57:1248–1251.

C.10. How would you deal with problems related to clamping of the pulmonary artery?

To assess the cardiopulmonary response to diverting the entire cardiac output through one lung, progressive occlusion of the vessel is first performed manually (Fig. 4.2). Careful assessment of right ventricular function is performed with transesophageal

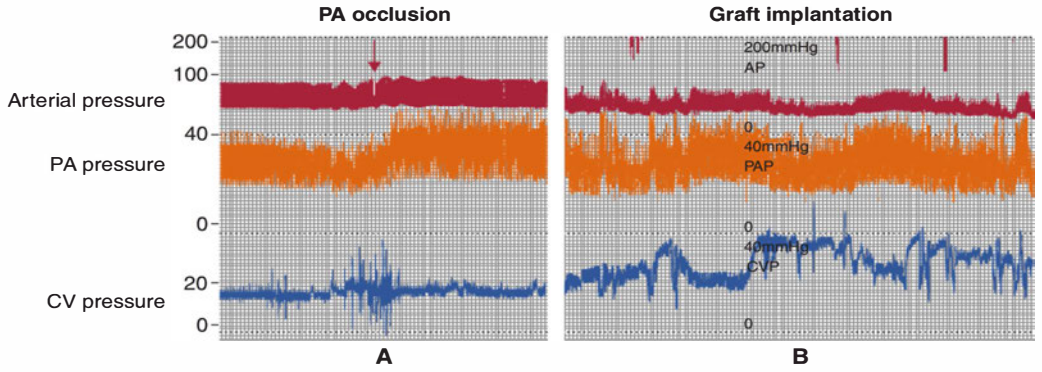

Figure 4.2 Tracings of femoral arterial blood pressure, along with pulmonary artery (PA) and central venous (CV) pressures, before and after occlusion of the left pulmonary artery (**A**) and during implantation of a left lung graft (**B**). (All pressures are in millimeters of mercury.)

echocardiography looking for evidence of right ventricular distention or hypokinesis. If well tolerated, the vessel is then clamped and stapled. If occlusion is poorly tolerated, the vessel is unclamped and a pulmonary vasodilator such as prostaglandin E_1 or iNO administered or positive inotropic infusion initiated. If severe respiratory or cardiovascular derangement persists after reclamping of the vessel despite pharmacologic intervention, heparin is administered and CPB instituted to avoid profound hypoxia or right ventricular failure. Nevertheless, for most patients undergoing single-lung transplantation, hypoxemia during single-lung ventilation and after pulmonary artery clamping is rarely a problem and right ventricular performance can be adequately maintained.

Triantafillou AN, Heerdt PM, Patterson GA. Lung transplantation. In: Youngberg JA, Lake CA, Roizen MF, et al, eds. *Cardiac, Thoracic and Vascular Anesthesia*. New York: Churchill Livingstone; 2000:703.

C.11. What hemodynamic alterations would you expect during graft implantation and reperfusion? How would you correct them?

During the process of performing the vascular and bronchial anastomoses, major disturbances on cardiac filling and rhythm can be produced (Fig. 4.2). Although often transient, systemic hypotension and pulmonary hypertension can ensue. Transient hypotension may follow the introduction of the vasodilator-containing lung graft preservatives into the systemic circulation. Incomplete removal of air from the lung can cause coronary artery air embolism, leading to transient myocardial ischemia. The latter is manifested by ST-segment elevation and regional wall motion abnormalities on transesophageal echocardiography. This condition is typically responsive to intravenous nitroglycerin while maintaining perfusion pressures with pressors. After reperfusion and subsequent ventilation of the new lung, pulmonary artery pressures and arterial blood gases should be closely monitored. Pulmonary artery pressure usually falls after reperfusion of the donor organ. If a substantial decrease is not observed, potential causes include anastomotic problems with the atrial cuff or the pulmonary artery. When pulmonary anastomotic problems are suspected, the surgeon should palpate to assess whether the pulmonary artery catheter is located proximal or distal to the anastomosis.

If a proximal location is confirmed, direct measurement of pulmonary artery pressures should be performed with a needle connected to pressure tubing handed off the operative field. Assessment of the pulmonary artery and venous flow pattern by transesophageal echocardiography can sometimes be of benefit in evaluating the adequacy of the anastomoses. Early graft dysfunction can manifest shortly after reperfusion of the first lung and may be the result of various insults. Occurring in 15% to 50% of cases, early graft dysfunction ranges in severity from modest chest radiograph abnormalities and increased inspired oxygen requirements to fulminant pulmonary edema with hypoxia and cardiovascular compromise. Immediate treatment includes adjustment of ventilation, addition of PEEP, and pulmonary vasodilators. iNO may be effective for improving oxygenation and reducing pulmonary artery pressures, and some clinicians advocate prophylactic iNO administration, although benefit of this intervention has recently been questioned. Should graft dysfunction become evident after implantation of the first lung, but before completion of the second lung transplantation, consideration should be given to initiating CPB. When severe hypoxemia persists after lung transplantation despite maximal medical therapy, including the use of iNO, extracorporeal membrane oxygenation (ECMO) may be indicated because primary graft dysfunction is the most frequent cause of perioperative mortality following lung transplantation.

Date H, Triantafillou AN, Trulock EP, et al. Inhaled nitric oxide reduces human allograft dysfunction. *J Thorac Cardiovasc Surg*. 1996;111:913–919.

Myles PS. Pulmonary transplantation. In: Kaplan JA, Slinger PD, eds. *Thoracic Anesthesia*. Philadelphia: Elsevier Science; 2003:295–314.

Perrin G, Roch A, Michelet P, et al. Inhaled nitric oxide does not prevent pulmonary edema after lung transplantation measured by lung water content: a randomized clinical study. *Chest*. 2006;129:1024–1030.

Pitcher DV, Snell GI, Scheinkestel CD, et al. High donor age, low donor oxygenation, and high recipient inotrope requirements predict early graft dysfunction in lung transplant recipients. *J Heart Lung Transplant*. 2005;24:1814–1820.

Prekker ME, Herrington CS, Hertz MI, et al. Early trends in PaO_2/fraction of inspired oxygen ratio predict outcome in lung transplant recipients with severe primary graft dysfunction. *Chest*. 2007;132:991–997.

Trulock EP. Lung transplantation. *Am J Respir Crit Care Med*. 1997;155:789.

C.12. When is cardiopulmonary bypass (CPB) necessary for lung transplantation?

CPB may be used electively for patients with severe pulmonary artery hypertension in whom double-lumen endobronchial tubes cannot be placed, or when visualization of hilar structures is poor. Nevertheless, in the absence of intraoperative complications, CPB is not desired because it can increase bleeding and blood product usage. It has also been suggested that CPB may aggravate postoperative lung dysfunction, although this has not been evident in cases in which lung transplantation was performed in conjunction with cardiac surgery. Nonetheless, the use of CPB has been associated with longer duration of mechanical ventilation and hospitalization, although it is difficult to differentiate whether the latter results directly from CPB or is the result of a complicated procedure that resulted in the need for it. Indications for CPB include right ventricular dysfunction not responding to medical therapy, early graft dysfunction occurring during implantation of the second lung during bilateral procedures, and surgical misadventures. Unplanned CPB is reported to occur in 12% to 46% of lung transplantation procedures, but predicting which patients may require this intervention is extremely difficult. Some report that CPB is more likely to be necessary for restrictive lung diseases than obstructive diseases.

In an attempt to derive the benefits of CPB while reducing complications, some centers advocate the use of heparin-bound ECMO systems. This approach allows for pulmonary support both during and after the procedure with minimal systemic anticoagulation.

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Dalibon N, Geffroy AN, Moutafis M, et al. Use of cardiopulmonary bypass for lung transplantation: a 10-year experience. *J Cardiothorac Vasc Anesth.* 2006;20:668–672.

de Hoyos A, Demajo W, Snell G, et al. Preoperative prediction for the use of cardiopulmonary bypass in lung transplantation. *J Thorac Cardiovasc Surg.* 1993;106:787–795.

Gammie JS, Lee JC, Pham SM, et al. Cardiopulmonary bypass is associated with early allograft dysfunction but not death after double-lung transplantation. *J Thorac Cardiovasc Surg.* 1998;115:990–997.

Lau CL, Hoganson DM, Meyers BF, et al. Use of an apical heart suction device for exposure in lung transplantation. *Ann Thorac Surg.* 2006;81:1524–1525.

Parekh K, Meyers BF, Patterson GA, et al. Outcome of lung transplantation for patients requiring concomitant cardiac surgery. *J Thorac Cardiovasc Surg.* 2005;130:859–863.

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Wang Y, Kurichi JE, Blumenthal NP, et al. Multiple variables affecting blood usage in lung transplantation. *J Heart Lung Transplant.* 2006;25:533–538.

C.13. Should fluid administration be restricted, and are blood products commonly required?

The amount of crystalloid that can be safely administered intraoperatively without adversely affecting the graft appears to be widely variable. Although efforts should be made to minimize fluid infusion intraoperatively, many patients undergoing lung transplantation require large amounts to maintain hemodynamic stability. Not uncommonly, central venous and pulmonary capillary wedge pressures of 3 to 5 mm Hg immediately after a transplantation are evident despite infusion of large amounts of crystalloid and colloid, as well as only moderate blood loss. The transplanted lung is at risk for pulmonary edema as a result of lack of lymphatic drainage and inflammatory insults, direct pulmonary trauma, and inflammatory cytokine release associated with reperfusion and organ harvest. The incidence of postoperative reperfusion pulmonary edema is described as 10% to 35%. Some reports suggest the practice of fluid restriction and low central venous pressures. In one study, central venous pressures greater than 7 mm Hg are correlated with longer intensive care unit stays and higher mortality.

Before the development of the bilateral lung transplantation procedure without CPB, patients with a history of surgery involving the lung or pleura or chronic infectious lung diseases were not deemed acceptable candidates for lung transplantation because of the anticipated excessive bleeding associated with dissecting a scarred lung after anticoagulation for CPB. Now, without the uniform requirement for heparinization, such patients are generally regarded as operative candidates. As with other surgical procedures in which hemorrhage is anticipated, continuous infusion of an antifibrinolytic has been proposed to reduce intraoperative bleeding in patients with cystic fibrosis or a history of previous intrathoracic surgery. Variables reported to increase the need for blood product usage include the use of CPB, double-lung procedures, and patients with cystic fibrosis. Transfusion therapy should remain a team decision and warrants a discussion between members of both the anesthesiology and

surgical staff. If blood products are to be administered, the anesthesiologist must know whether the patient has antibodies to cytomegalovirus and must closely check blood products to confirm they coincide with the patient's status.

Bigham M, Dickstein ML, Hogue CW Jr. Cardiac and lung transplantation. In: Estafanous FG, Barash PG, Reves JG, eds. *Cardiac Anesthesia*. Philadelphia: Lippincott Williams & Wilkins; 2001:636.

Myles PS. Pulmonary transplantation. In: Kaplan JA, Slinger PD, eds. *Thoracic Anesthesia*. Philadelphia: Elsevier Science; 2003:295–314.

Pilcher DV, Scheinkestel CD, Snell GI, et al. High central venous pressure is associated with prolonged mechanical ventilation and increased mortality after lung transplantation. *J Thoracic Cardiovasc Surg*. 2005;129:912–918.

Wang Y, Kurichi JE, Blumenthal NP, et al. Multiple variables affecting blood usage in lung transplantation. *J Heart Lung Transplant*. 2006;25:533–538.

C.14. Would you extubate the patient upon conclusion of the procedure?

Because of the cardiopulmonary insult associated with the procedure, the large postoperative volume shifts, hypothermia, and the frequent need for postoperative bronchoscopy, the trachea of lung transplant recipients is not generally extubated immediately after the procedure. Accordingly, unless intraoperative events (e.g., hyperinflation of the remaining intact lung) suggest that postoperative differential lung ventilation will be required, or unless functional issues such as profound oropharyngeal edema or difficult intubation are present, the double-lumen endotracheal tube is exchanged for a single-lumen tube. In many patients, the endotracheal tube change can be facilitated by use of an exchange catheter. Nonetheless, great care should be taken to not advance the catheter too far and damage the graft. It is often beneficial to perform fiberoptic bronchoscopy to examine bronchial anastomoses and aggressively suction secretions or blood after replacement of the double-lumen tube with a single-lumen endotracheal tube. As with many procedures, careful inspection of the upper airway for edema should be performed by laryngoscopy before exchange of the double-lumen endobronchial tube with a single-lumen endotracheal tube.

D. Postoperative Management

D.1. What are the major complications after lung transplantation?

Early graft dysfunction, episodes of rejection, infection, and airway complication are the major early complications of lung transplantation. Early graft dysfunction varies in severity from mild shunting and chest radiograph infiltrates to gross pulmonary edema. Management includes fluid restriction, diuretics, PEEP, iNO, and ECMO for severe cases. Immunosuppression is usually initiated before surgery, and the induction phase of therapy is continued for 5 to 10 days. The exact regimen varies among institutions but typically includes azathioprine, steroids, cyclosporine, and polyclonal antilymphocyte/antithymocyte globulins or interleukin-2 receptor antagonists. Acute rejection episodes are usually treated with intense steroid therapy and optimization of other immunosuppressant dosages. A challenge arises in differentiating acute rejection from infection as a source of shunting and chest radiograph infiltrates. Transbronchial biopsy is often necessary to make the distinction from histologic specimens. Bacterial pneumonia is the most frequent infection in the first 2 weeks. Although unusual in the first 2 weeks after transplantation, cytomegalovirus is the second most common source of infectious pneumonitis. Broad-spectrum antibiotics

are given perioperatively, and the regimen is adjusted based on the results of donor and recipient cultures. Antibiotic therapy for patients with cystic fibrosis is challenging, and the drug chosen is dictated by the patient's cultures and prior history of the organisms colonizing his or her lungs. Prophylactic acyclovir appears to be effective in reducing infections caused by herpes simplex, and trimethoprim-sulfamethoxazole is given to prevent infections from *Pneumocystis carinii*.

Myles PS. Pulmonary transplantation. In: Kaplan JA, Slinger PD, eds. *Thoracic Anesthesia*. Philadelphia: Elsevier Science; 2003:295–314.

Christie JS, Edwards LB, Aurora P, et al. The registry of the international society for heart and lung transplantation: twenty-six official adult lung and heart-lung transplantation report—2009. *J Heart Lung Transplant*. 2009;28:1031–1049.

D.2. How is postoperative ventilation managed, and for how long is it required?

After most procedures, the fraction of inspired oxygen (F_{IO_2}) can be rapidly reduced, and weaning from the ventilator can be initiated as soon as the patient is warm and stable. An exception to this approach is the patient who has undergone single-lung transplantation for pulmonary hypertension. Because of a propensity for episodes of cardiopulmonary instability during the first 24 to 48 hours postoperatively, it is advantageous to keep these patients mechanically ventilated during this period, although increasing experience is revealing the positive effects of rapid weaning protocols in those patients who tolerate it.

Postoperatively, ventilation–perfusion mismatch and intrapulmonary shunt are often more pronounced after single-lung transplantation than bilateral lung transplantation. Not surprisingly, patients with restrictive disease usually display the best pulmonary function after single-lung transplantation, because the graft receives the majority of both ventilation and perfusion. Alternatively, after single-lung transplantation in patients with emphysema, the remaining native lung often receives a substantial portion of the tidal volume, whereas in patients with pulmonary hypertension, the native lung continues to be ventilated but receives very little blood flow. On rare occasions, differential ventilation of the transplanted and native lung is needed after single-lung transplantation for obstructive lung disease. In these situations, the double-lumen endobronchial tube is left in place and two ventilators are employed. The native lung is ventilated with low tidal volume (2 to 3 mL/kg) and rate, or even just connected to CPAP without intermittent mandatory ventilation. Nonetheless, the condition usually resolves rapidly with return of spontaneous ventilation. Postural changes in arterial oxygen saturation are often prominent in single-lung transplant recipients. In general, patients who received a single lung for pulmonary hypertension or emphysema display better postoperative pulmonary function with the "transplant side up," whereas the opposite may be true in certain patients with restrictive lung disease. The precise etiology of this response is unclear but probably reflects positional variation in ventilation-perfusion matching.

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D.3. What special precautions should be taken when a lung transplant recipient requires general anesthesia for subsequent nonpulmonary surgery?

In general, after lung transplantation, the patient can be treated like any other ill immunocompromised patient. Recipients have subsequently undergone various surgical procedures unrelated to their pulmonary disease after lung transplantation and had few anesthetic problems. Not surprisingly, differences in the compliance and expiratory flow rates of a native and transplanted lung after single-lung transplantation for emphysema can result in alterations in intraoperative capnography. This phenomenon has been described as producing a biphasic pattern of carbon dioxide exhalation, with the first peak reflecting exhalation from the transplanted lung and the second peak exhalation from the native lung. In addition, the transplanted lung is denervated so the cough reflex is present only in the proximal native airway and mucociliary function is impaired. In contrast, hypoxic pulmonary vasoconstriction is intact after lung transplantation and central respiratory control is unaffected. Nevertheless, a blunted response to carbon dioxide may persist for patients with preoperative hypercapnia.

The major factor limiting long-term survival from lung transplantation is bronchiolitis obliterans syndrome. This progressive condition characterized by progressive narrowing of small airways must be considered in patients with prior lung transplantation presenting for surgery and anesthesia after the initial recovery phase. Other perioperative considerations for the patient with a prior lung transplant undergoing subsequent surgery are based on whether the patient was the recipient of one or two lungs. In the former case, ventilation and perfusion of the remaining diseased native lung is influenced by the functional status of the transplanted lung. For patients with obstructive lung disease, overinflation of the native lung and resultant mediastinal shift with associated ventilation and hemodynamic consequences, although rare, must be considered when employing positive pressure ventilation.

Although these patients should be assessed with the vigilance applied to patients without a history of transplantation, some points are noteworthy. Patients should be thoroughly evaluated to rule out the presence of an infection. Preoperative workup also should assess presence of renal dysfunction resulting from immunosuppressive therapy, presence of upper gastrointestinal bleeding from gastritis or peptic ulcer disease, and hepatobiliary or pancreatic dysfunction, because these are common after transplantation. Perioperative medications may also include a variety of antibiotic regimens, "stress-dose" steroids, and β-agonists because these patients may be more prone to bronchoconstriction. Aspiration precautions should also be implemented.

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Cerza RA. Cardiopulmonary bypass in a post-lung transplant patient. *J Cardiothorac Vasc Anesth*. 1996;10:384–386.

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D.4. What are the long-term outcomes of lung transplantation?

Increased experience and improved techniques have made lung transplantation a realistic option for many patients. Nevertheless, the procedure is not without substantial risk and a favorable outcome is by no means ensured. Data suggest that survival after lung transplant is better in patients with cystic fibrosis, IPAH, sarcoidosis, and alpha antitrypsin (AAT) deficiency compared with COPD and idiopathic pulmonary fibrosis (IPF). This may be due to the fact that patients with COPD and IPF are older and have more comorbidities. Since 2009, 3-month and 1-, 3-, 5-, and 10-year survival rates after lung transplantation are 89%, 79%, 64%, 52%, and 29%, respectively. According to the registry data, the improvement in survival can be attributed to improvements in 1-year survival. Most patients who underwent bilateral lung transplantation demonstrated better survival compared with single-lung transplantation in all disease categories. Interestingly, malignancies (lymphomas early and then skin malignancies later) accounted for 12% of all deaths between 5 and 10 years after transplantation. The major cause of early mortality is graft dysfunction and noncytomegalovirus infection, and the major causes of late mortality are noncytomegalovirus infection, bronchiolitis obliterans syndrome, and rejection. Survival rates differed significantly by age, with lower short- and long-term survival in age-groups greater than 50 years of age.

Christie JS, Edwards LB, Aurora P, et al. The registry of the international society for heart and lung transplantation: twenty-sixth official adult lung and heart-lung transplantation report—2009. *J Heart Lung Transplant.* 2009;28:1031–1049.

D.5. Are there surgical alternatives to lung transplantation?

Some patients with severe emphysema who are not deemed transplant candidates may benefit from lung volume reduction surgery (LVRS) or "reduction pneumoplasty." Performed either through a median sternotomy or a bilateral thoracoscopy, the goal of LVRS is to remove up to 30% of the patient's most severely compromised lung tissue. Postoperatively, this allows the previously hyperexpanded chest and depressed diaphragm to resume a more normal shape, thereby improving chest wall mechanics and eventually pulmonary function. Nevertheless, beneficial effects of the procedure are not immediately evident, usually requiring 1 to 2 months. Furthermore, whether the improvement in pulmonary function is sufficient to warrant the risk of the procedure remains controversial. Recent data indicate that for many patients, LVRS represents a viable alternative to transplantation.

Henrique C, Boasquevisque R, Yildirim E, et al. Surgical techniques: lung transplant and lung volume reduction. *Proc Am Thorac Soc.* 2009;6:66–78.

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SECTION II

The Cardiovascular System

CHAPTER 5

Ischemic Heart Disease and Coronary Artery Bypass Grafting

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A 57-YEAR-OLD MAN

with triple-vessel coronary artery disease (CAD) was scheduled for coronary artery bypass grafting (CABG). He had a myocardial infarction (MI) 7 months ago. He was taking nitroglycerin, digoxin, metoprolol, isosorbide dinitrate (Isordil), and nifedipine. His blood pressure (BP) was 120/80 mm Hg and his heart rate (HR) was 60 beats per minute.

A. Medical Disease and Differential Diagnosis

1. What is triple-vessel CAD? Name the branches of the coronary arteries.
2. What are the indications for CABG?
3. What is percutaneous coronary intervention (PCI)? Discuss its indications, contraindications, and results.
4. What are the results of CABG?

B. Preoperative Evaluation and Preparation

1. Which preoperative tests would you order?
2. How would you evaluate the patient's left ventricular function?
3. What are the three major determinants of myocardial oxygen consumption? How are they measured clinically?

4. Which factors determine myocardial oxygen supply?
5. Would you discontinue digoxin? Why? What is its half-life?
6. Would you discontinue the β-blocker (metoprolol)? Why? What is its half-life? What is the role of β-adrenergic blockers in treating congestive heart failure (CHF)?
7. If the patient who is on metoprolol develops hypotension intraoperatively, how would you manage it?
8. What is nifedipine? How does it work?

C. Intraoperative Management

C.I. *Before Cardiopulmonary Bypass*

1. How do you monitor the patient?
2. What is the Allen test?
3. Should you monitor temperature from multiple sites?
4. How do you know that the tip of the pulmonary artery (PA) catheter is in the right ventricle (RV) or the PA?
5. What is normal pulmonary artery occlusion pressure (PAOP)?
6. Is it necessary to monitor PA pressure for coronary artery operations?
7. What are the complications of PA catheterization?
8. What are the hemodynamic consequences of myocardial ischemia (MI)? How can you detect MI? Is PAOP a sensitive indicator of MI?
9. How would you monitor electrocardiogram (ECG)? Why V_5? If you do not have precordial leads in your ECG machine, how can you monitor the left ventricle (LV)?
10. Discuss the principles and clinical applications of intraoperative transesophageal two-dimensional echocardiography.
11. How would you induce anesthesia?
12. How would you maintain anesthesia?
13. What is the better anesthetic agent for this operation—an inhalation or intravenous agent?
14. What are the cardiovascular effects of halothane, enflurane, isoflurane, desflurane, sevoflurane, morphine, and fentanyl?
15. Is isoflurane dangerous for the patient with CAD?
16. What is the cardiovascular effect of nitrous oxide (N_2O)?
17. What kind of muscle relaxant would you use? Why?
18. If ST-segment depression is seen during surgery, how would you treat it? What is the relation between perioperative myocardial ischemia and postoperative MI?
19. Would you use prophylactic nitroglycerin during CABG to prevent intraoperative myocardial ischemia or perioperative MI?
20. How would you correct hypertension?
21. How would you treat hypotension?
22. What are the indications for intravenous metoprolol, labetalol, or esmolol during surgery? How much would you give? What are the relative contraindications?
23. How would you correct increased PAOP?
24. What should you do during sternal splitting?
25. Would you monitor PAOP continuously? Why?
26. Discuss autologous transfusion and blood conservation for cardiac surgery.

C.II. *During Cardiopulmonary Bypass*

1. What anticoagulant would you give before cardiopulmonary bypass (CPB)? How much would you give? What is its mechanism?
2. What is the half-life of heparin? How is it eliminated?
3. How do you monitor heparin dosage? What is the activated coagulation time (ACT) test?
4. What is total CPB? What is partial bypass?
5. What is the purpose of venting the LV? How can it be done?
6. How many types of oxygenators are there? What are the advantages of each type?
7. What kind of priming solution would you use? How much priming solution would you use? When would you prime with blood? Why?
8. What are the advantages and disadvantages of hemodilution?
9. What kind of pumps do you use? Are they pulsatile or not?
10. How do you monitor the patient during CPB?
11. How much BP would you keep during CPB? Why?
12. How would you treat hypotension during CPB?
13. How would you treat hypertension (a mean arterial pressure [MAP] of over 100 mm Hg)?
14. How do you prepare an intravenous infusion of sodium nitroprusside, nicardipine, and nitroglycerin? What are the usual doses? Which do you prefer to use?
15. How much pump flow would you maintain during CPB?
16. How would you adjust the pump flow during hypothermia?
17. How would you adjust the pump flow during hemodilution?
18. What are the advantages of hypothermia? Does hypothermia offer neuroprotection?
19. How does blood viscosity change during hypothermia and hemodilution?
20. What are the main causes of death associated with accidental hypothermia?
21. Would you give anesthesia during CPB? Why?
22. Would you give muscle relaxants during CPB? How is the action of muscle relaxant affected during CPB?
23. How do you know the patient is well perfused during CPB?
24. How much gas flow would you use for the oxygenator? What kind of gas would you use? Why?
25. What are the disadvantages of hypocapnia during CPB?
26. The arterial blood gases and electrolytes during CPB are as follows: pH, 7.36; $Paco_2$, 42 mm Hg; Pao_2, 449 mm Hg; CO_2 content, 24 mEq per L; Na, 128 mEq per L; K, 5.8 mEq per L; and Hct, 20%. The patient's temperature is 27° C (80.6° F). At what temperature are blood gases measured? How would you correct the blood gases according to patient's body temperature? Would you treat the arterial blood gases at 37° C (98.6° F) or at patient's body temperature?
27. If the blood level of the venous reservoir is low, what would you replace it with? Blood or balanced salt solution?
28. How do you estimate the fluid balance during CPB?
29. How would you preserve the myocardium during CPB?
30. What is the cardioplegic solution? How much would you use?
31. For how long a period can the aorta be cross-clamped?

32. Why would urine become pink in some cases of CPB? What is the renal threshold for plasma hemoglobin?
33. At what temperature can the patient be weaned from CPB?
34. Why does it take longer to rewarm than to cool the patient by the pump oxygenator?
35. How would you defibrillate the heart internally during CPB?
36. Why is calcium chloride usually administered right before the patient comes off the pump?
37. If the HR is 40 beats per minute, what should you do?
38. How does the blood sugar level change during CPB? Why? Does hyperglycemia increase neurologic complications during CPB?
39. What are the effects of CPB on platelet and coagulation factors?
40. How would you prepare for termination of CPB?
41. How would you decide the need for inotropic support?

C.III. *After Cardiopulmonary Bypass*

1. How would you reverse heparin? How much protamine would you use? What are the other drugs used to neutralize heparin?
2. What is the action mechanism of protamine?
3. What are the complications of too much protamine?
4. Why did the patient develop hypotension after protamine was administered? How do you treat and prevent this condition?
5. What are the indications for intra-aortic balloon pump (IABP)?
6. What are the principles of IABP?
7. What are the complications of IABP?
8. Can PAOP represent left ventricular end-diastolic volume (LVEDV) after CABG?

D. Postoperative Management

1. What are the postoperative complications?
2. Would you reverse the muscle relaxants? Why?
3. When will you wean the patient from the respirator?
4. What criteria would you use in deciding when to wean the patient from the respirator?

A. Medical Disease and Differential Diagnosis

A.1. What is triple-vessel CAD? Name the branches of the coronary arteries.

Triple-vessel CAD involves progressive atherosclerosis of the major branches of the coronary arteries with eventual luminal obstruction and myocardial injury. The intimal disease is typically segmental but can be diffuse in severe cases. The coronary arteries are the following:

- The right coronary artery (RCA)
- The left anterior descending (LAD) branch of the left main coronary artery
- The left circumflex (CFX) branch of the left main coronary artery

The branches of coronary arteries are shown in Figure 5.1. The LAD and CFX arise from the left main coronary artery (LMCA). The sinus node is supplied by the RCA in approximately 50% to 60% of human beings and by the left CFX artery in the remaining 40% to 50%. The atrioventricular (AV) node is supplied by the RCA in 85%

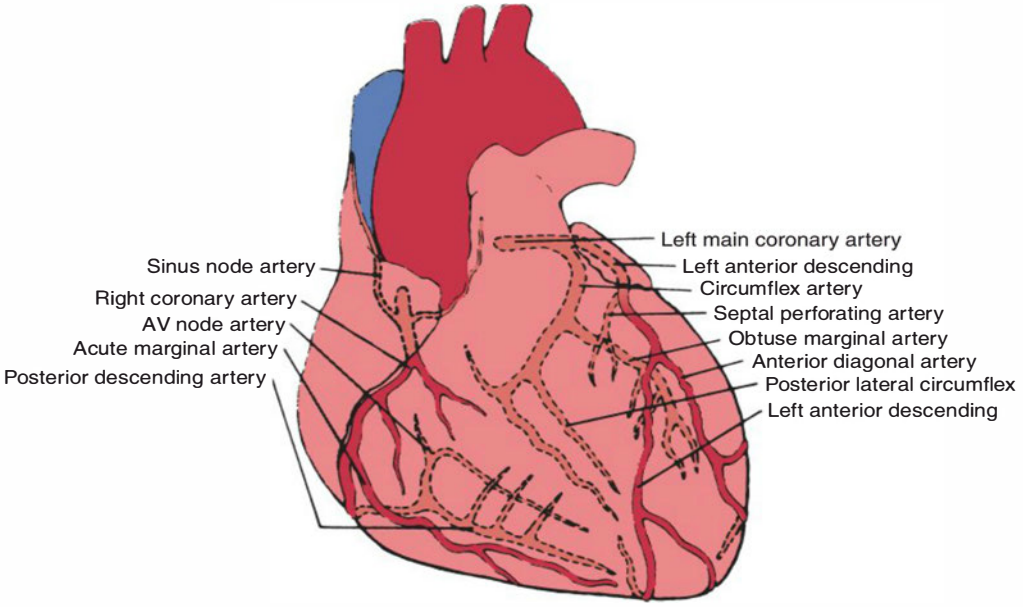

Figure 5.1 Branches of the coronary arteries.

to 90% of humans and by the left CFX artery in the remaining 10% to 15%; therefore, the RCA is dominant in 85% to 90% of patients. The most common arteries for coronary bypass grafting are LAD, obtuse marginal (branch of CFX), and posterior descending (branch of RCA) arteries.

Libby P, Bonow RO, Mann DL, et al., eds. *Braunwald's Heart Disease, A Textbook of Cardiovascular Medicine.* 8th ed. Philadelphia: Saunders Elsevier; 2008:465.

A.2. What are the indications for CABG?

The indications for CABG are the need for improvement of the quality or duration of life. Patients whose angina is not controlled by medical treatment or who have unacceptable side effects with such management should be considered for coronary revascularization.

The candidates for CABG are usually older patients with more diffuse CAD and decreased left ventricular function. The indications for CABG are as follows:

- Unstable angina pectoris or episodes of prolonged myocardial ischemia
- Persistent angina pectoris, despite optimal medical therapy
- Repeated episodes of myocardial ischemia following MI
- Prinzmetal angina (variant angina) with coronary artery obstruction
- High-grade LMCA obstruction, double- or triple-vessel obstruction, or proximal LAD artery obstruction
- Acute MI, cardiogenic shock, intractable ventricular arrhythmias
- Stable angina pectoris that interferes with desired lifestyle

Libby P, Bonow RO, Mann DL, et al., eds. *Braunwald's Heart Disease, A Textbook of Cardiovascular Medicine.* 8th ed. Philadelphia: Saunders Elsevier; 2008:1353.

A.3. What is percutaneous coronary intervention (PCI)? Discuss its indications, contraindications, and results.

PCI has developed rapidly since its introduction by Gruentzig in 1977. It is now an acceptable method of treating selected patients who have angina pectoris. This technique involves the passage of a small (3 French) catheter into the involved coronary artery and through the stenosis. With the balloon portion of the catheter straddling the stenosis, inflations are performed that result in enlargement of the stenotic lumen. The luminal widening is achieved by a controlled injury involving, to a varying degree, plaque compression, intimal fissures, and medial stretching. Next, coronary stents are introduced to maintain long-term patency. The stents are either bare-metal (cobalt–chromium alloy) or drug-eluting stents (DES).

PCI has redefined who is candidate for elective surgical myocardial revascularization. The indications for PCI have changed during the recent past. With the current available technology, PCI is considered a therapeutic option in any individual with disabling ischemic symptoms despite good medical therapy and focal obstructive coronary disease regardless of cause. The indications for PCI are as follows:

- Isolated discrete proximal single-vessel disease
- Proximal double-vessel disease
- Post-CABG with new stenotic lesions or stenosis at distal anastomosis
- Restenosis following PCI
- Contraindications to CABG
- Coronary stenosis following cardiac transplantation
- Occluded vessels within the last 6 months and less than 15 mm in length
- Poststreptokinase therapy for revascularization

PCI is contraindicated in the following:

- Left main CAD in which the distal vessels are not protected by at least one completely patent large collateral vessel
- Multivessel disease with severe diffuse arteriosclerosis
- Absence of a discrete obstructing lesion
- Absence of a formal cardiac surgical program within the institution

The results of PCI are as follows: The primary success rate is approximately 90%. The primary weakness of the procedure is restenosis, at a rate of approximately 30%, 6 months after the procedure. Dilatation can be repeated with a 90% success rate. The artery tends to remain patent after the second angioplasty. With the introduction of coronary stents, which act as a metal scaffold, the restenosis rate after PCI has been decreasing, and fewer patient require subsequent revascularization: 10% to 15% after stenting versus 25% to 35% after PCI alone. The largest decrease in luminal diameter following stent placement is evident within the first 6 to 9 months after stent placement and is the result of proliferative neointimal tissue growth in response to the associated injury and inflammation. Recently, pharmacologic agents (sirolimus, an immunosuppressant, and paclitaxel, an antineoplastic) are coupled with polymers that elute or slowly release these inhibitors from the stent surface. The DES have reduced the need for target-lesion revascularization to an even lower rate, 4% to 6%.

However, the PCI is a different therapeutic approach than CABG. PCI is targeting the area of lesion only, whereas CABG bypass targets not only the existing, but future lesion areas. This may be the reason that, at least in the intermediate term, CABG is considered to be superior for patients with multivessel disease.

Diegeler et al. showed that, for isolated high-grade lesions of the LAD, CABG through a left anterior thoracotomy is as effective as PCI with stent placement. Although stenting provided excellent short-term results with fewer periprocedural

adverse events, CABG was superior with regard to the need for repeated intervention in the target vessel and freedom from angina at 6 months of follow-up. Further, Serruys et al. compared outcomes between PCI with stent and CABG surgery and found that at 5 years, there was no difference in mortality between stenting and surgery for multivessel disease. Importantly, the incidence of stroke or MI was not significantly different between the two groups. However, overall freedom from major adverse cardiac and cerebrovascular events was higher in the stent group, driven by the increased need for repeat revascularization. A recent report on 10-year outcomes also showed that for the treatment of unprotected LMCA disease, PCI with stent implantation showed similar long-term mortality and rates of death, Q-wave MI, or stroke. However, stenting, even with DES, was associated with higher rates of repeat revascularization than was CABG. Lastly, a recent comparison between stenting and CABG in patients with previously untreated three-vessel disease or LMCA disease concluded that CABG remains the standard of care for patients with three-vessel or LMCA disease, since the use of CABG, as compared with PCI, resulted in lower rates of the combined end point of major adverse cardiac or cerebrovascular events at 1 year.

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Libby P, Bonow RO, Mann DL, et al., eds. *Braunwald's Heart Disease, A Textbook of Cardiovascular Medicine.* 8th ed. Philadelphia: Saunders Elsevier; 2008:1301.

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Serruys P, Morice M, Kappetein P, et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. *N Engl J Med.* 2009;360:961–972.

Serruys P, Ong A, Herdweden L, et al. Five-year outcomes after coronary stenting versus bypass surgery for the treatment of multivessel disease. *J Am Coll Cardiol.* 2005;46:575–581.

A.4. What are the results of CABG?

Kuan et al. reported a perioperative MI rate of 4% to 6%. The overall operative mortality rate of CABG at major medical centers is approximately 1%. Reoperation is associated with a higher operative mortality, approximately 2% to 3%. Rahimtoola et al. studied the status of patients who underwent CABG for unstable angina over a 10-year period. The 1-month mortality rate was 1.8%. The 5-year survival rate was 92%, and the 10-year survival rate was 83%. CABG was repeated at a rate of 1% to 2% per year; 81% of patients were angina-free or had only mild angina. Loop et al. found that the 10-year survival rate among the group receiving the internal mammary artery graft, as compared with the group receiving the vein grafts (exclusive of hospital deaths), was 93.4% versus 88% for those with one-vessel disease; 90.0% versus 79.5% for those with two-vessel disease; and 82.6% versus 71.0% for those with three-vessel disease. At the end of the first 10 postoperative years, the patency of internal mammary artery grafts is 85% to 95%, whereas the patency of saphenous vein grafts is only 38% to 45%.

A systematic overview of the seven randomized trials that compared coronary bypass surgery with medical therapy between 1972 and 1984 yielded 2,649 patients.

Patients undergoing CABG had a significantly lower mortality at 5, 7, and 10 years, but by 10 years, 41% of the patients initially randomized to medical therapy had undergone CABG. Therefore, coronary bypass surgery prolongs survival in patients with significant left main CAD (irrespective of symptoms), in patients with multivessel disease and impaired left ventricular function, and in patients with three-vessel disease that includes the proximal LAD coronary artery (irrespective of left ventricular function). Surgical therapy also has been demonstrated to prolong life in patients with two-vessel disease and left ventricular dysfunction, particularly in those with a critical stenosis of the proximal LAD coronary artery. Although no study has documented a survival benefit with surgical treatment in patients with single-vessel disease, there is some evidence that such patients who have impaired left ventricular function have a poor long-term survival rate with medical therapy alone. Such patients with angina and/or evidence of ischemia at a low or moderate level of exercise, especially those with obstruction of the proximal LAD coronary artery, may benefit from coronary revascularization by either angioplasty or bypass surgery.

Hannah et al. studied prospectively 37,212 patients who underwent CABG, and 22,102 patients who underwent stenting; CABG was associated with a significantly higher likelihood of survival (hazard ratios for death 0.75 for two- and 0.64 for three-vessel CAD, compared with stenting). The CABG patients had significantly lower median ejection fractions, were more likely than patients who received stents to have had an MI in the week before the procedure, had a significantly higher prevalence of numerous coexisting conditions, and were significantly more likely to have three-vessel disease.

More recently, use of perioperative statin therapy appears to significantly reduced mortality outcomes in patients undergoing CABG surgery. Magoven et al., reported an operative mortality of 2.4% for all patients, 1.7% for statin users and 2.8% for non-statin users ($P < .07$). According to multivariate analysis, lack of statin use was found to be an independent predictor of mortality in high-risk patients (n = 245, 12.9% vs. 5.6%, $P < .05$).

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Haase J, Jung T, Storger H, et al. Long-term outcome after implantation of bare metal stents for the treatment of coronary artery disease: rationale for the clinical use of antiproliferative stent coatings. *J Interv Cardiol.* 2003;16(6):469–473.

Hannah EL, Racz MJ, Walford G, et al. Long-term outcomes of coronary-artery bypass grafting versus stent implantation. *N Engl J Med.* 2005;352:2174–2184.

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Lytle BW, Loop FD, Cosgrove DM, et al. Long-term (5 to 12 years) serial studies of internal mammary artery and saphenous vein coronary bypass grafts. *J Thorac Cardiovasc Surg.* 1985;89:248–258.

Magovern J, Moraca R, Bailey S, et al. Preoperative statin is associated with decreased operative mortality in high risk coronary artery bypass patients. *J Cardiothor Surg.* 2010;5:8.

Rahimtoola SH, Nanley D, Grunckemeier G, et al. Ten-year survival after coronary bypass surgery. *N Engl J Med.* 1983;308:676.

B. Preoperative Evaluation and Preparation

B.1. Which preoperative tests would you order?

In addition to the routine systemic examinations of all organ systems, special attention should be paid to the cardiovascular status.

- Renal function—urinalysis, blood urea nitrogen, creatinine
- The routine evaluation of the hepatic function is not any more the standard, unless specifically indicated, that is, previous history of hepatitis or jaundice or the patient is drug abuser.
- Pulmonary function—chest x-ray film (absolutely indicated in reoperated sternotomies to investigate the proximity of the sternum to the anterior surface of the heart), baseline arterial blood gases, and spirometry if indicated.
- Hematologic function—complete blood count, prothrombin time, partial thromboplastin time, platelets (platelet function if available and/or indicated; namely, for those patients previously receiving antiplatelet therapy)
- Metabolism—electrolytes and blood sugar
- Cardiovascular function—resting and exercise ECG (if a stress test was performed preoperatively), cardiac catheterization and coronary angiography, location and severity of coronary occlusion, echocardiography, and left ventricular function (from catheterization, magnetic resonance imaging, enhanced multidetector CT, and/or echocardiography).

B.2. How would you evaluate the patient's left ventricular function?

- Medical history—presence or absence of MI and angina
- Symptoms and clinical signs of left ventricular failure (dyspnea at rest or exercise, nocturnal orthopnea) and/or right heart failure (ascites, pitting edema, jugular vein distention)
- Cardiac catheterization, angiography, and echocardiography
- Ejection fraction (normally ~ 65%)
- Left ventricular end-diastolic pressure (LVEDP) or pulmonary artery occlusion pressure (PAOP: normal 6 to 15 mm Hg)
- Left ventricular wall motion—normal (wall thickening of >30%), hypokinesia (wall thickening of 10% to 30%), akinesia (wall thickening of <10%), or dyskinesia (outward motion during systole) (Fig. 5.2)
- Cardiac index (normal 2.2 to 3 L/min/m^2)
- Myocardial viability studies (contrast echocardiography or positron emission tomography study)
- End-systolic pressure volume relation from multiple pressure–volume loops

Abnormal regional wall motion (RWM), most commonly, is the result of CAD, which interrupts perfusion to fairly well-defined territories and hence results in abnormal motion in those segments. There is a gradation of wall motion abnormality that consists progressively of hypokinesis, akinesis, and, subsequently, dyskinesis in which a wall moves away from the center of the ventricle. Because wall thickening and endocardial motion are intrinsically tied, virtually all RWM abnormalities are expected initially to be associated with abnormalities of thickening as well as endocardial motion (see also Chapter 6, section A.3).

Libby P, Bonow RO, Mann DL, et al., eds. *Braunwald's Heart Disease, A Textbook of Cardiovascular Medicine*. 8th ed. Philadelphia: Saunders Elsevier; 2008:245.

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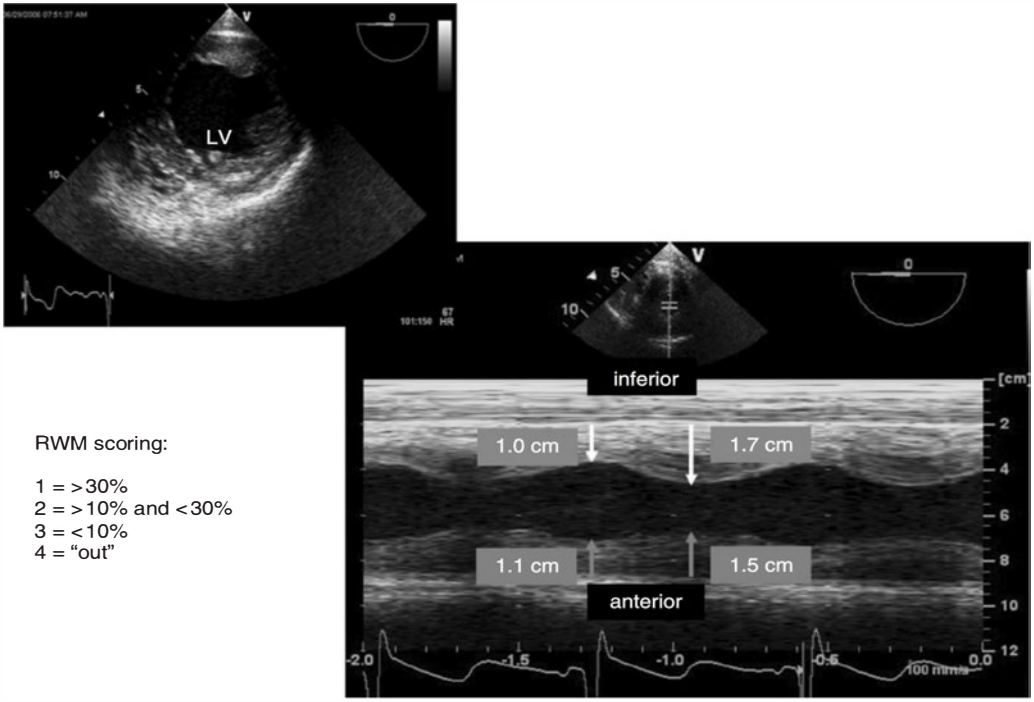


Figure 5.2 Echocardiographic evaluation of the left ventricle (LV). The transgastric mid-papillary short axis view of the left ventricle is shown in left. By placing a cursor line across the middle of the inferior (top of the image) and anterior (bottom of the image) segments of the left ventricular myocardium, the motion of the segments over time is shown in the right image. The percent wall thickening can be either visually estimated, or measured, between diastole and systole.

B.3. What are the three major determinants of myocardial oxygen consumption? How are they measured clinically?

The three major determinants of myocardial oxygen consumption are myocardial wall tension, contractility, and HR.

Myocardial wall tension is estimated by the following:

- The Laplace equation states that the wall tension (T) is analogous to the diameter of the ventricle (R, radius) and the intracavitary pressure (P) and inversely proportional to the myocardial wall thickness (Th): $T = P \times R \div 2Th$
- Preload—left ventricular end-diastolic volume (LVEDV), LVEDP, left atrial pressure, or PAOP
- Afterload—systolic ventricular pressure or systolic BP if there is no aortic stenosis

Contractility is measured by the following:

- *Invasive techniques.* Maximal velocity of contraction (Vmax), dP/dt (pressure time indices of ventricle: how fast [dt] the intraventricular pressure [dP] develops), or left ventricular end-systolic pressure/volume ratio
- *Noninvasive technique.* Preejection period/left ventricular ejection time, and global and regional ventricular wall motion by echocardiography (Fig. 5.3)

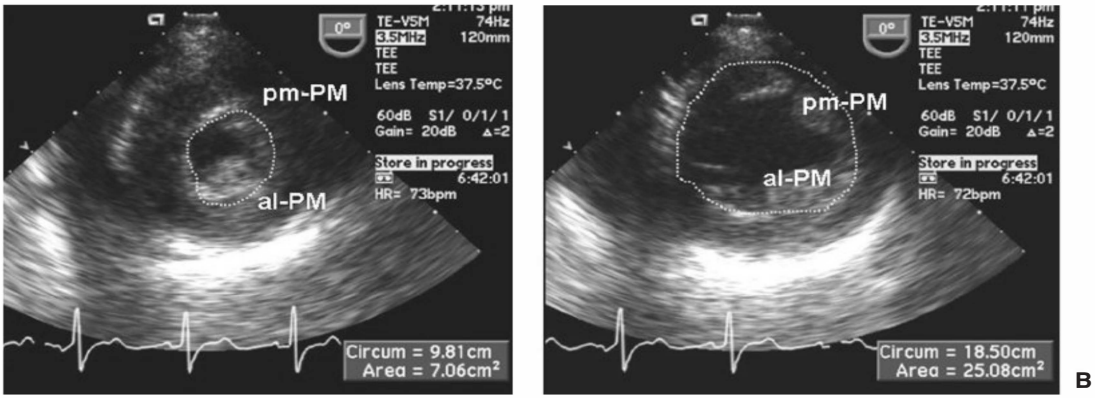


Figure 5.3 Echocardiographic evaluation of the systolic function of the left ventricle. The transgastric mid-papillary short-axis view of the left ventricle is shown in systole **(A)** and diastole **(B)**. The endocardial border is traced (without including the endocardium of the two papillary muscles), and the end-systolic (ESA) and end-diastolic (EDA) areas are calculated. The percentage area change (fractional area change [FAC]) is calculated as: FAC = (EDA − ESA)/EDA. The FAC correlates with, but does not substitute the percentage ejection fraction. al-PM, anterolateral papillary muscle; pm-PM, posteromedial papillary muscle.

Libby P, Bonow RO, Mann DL, et al., eds. *Braunwald's Heart Disease, A Textbook of Cardiovascular Medicine.* 8th ed. Philadelphia: Saunders Elsevier; 2008:1278.

O'Brien ERM, Nathan HJ. Coronary physiology and atherosclerosis. In: Kaplan JA, Reich DL, Savino JS, et al., eds. *Kaplan's Cardiac Anesthesia.* 6th ed. Philadelphia: Elsevier Saunders; 2011:132–156.

B.4. Which factors determine myocardial oxygen supply?

Myocardial oxygen supply = coronary blood flow × arterial oxygen content

The coronary blood flow depends on the following:

- Aortic diastolic pressure (DAP)
- LVEDP
- Patency of coronary arteries
- Coronary vascular tone

And it can be determined by the formula:

$$\text{Coronary blood flow} = \text{coronary perfusion pressure} \div \text{myocardial vascular resistance,}$$
$$\text{Or, (DAP} - \text{LVEDP)} \div \text{myocardial vascular resistance}$$

Arterial O_2 content is determined by the following equation:

$$Cao_2 = 1.34 \times \text{hemoglobin} \times O_2 \text{ saturation} + (0.0031 \times Pao_2)$$

O'Brien ERM, Nathan HJ. Coronary physiology and atherosclerosis. In: Kaplan JA, Reich DL, Savino JS, et al., eds. *Kaplan's Cardiac Anesthesia.* 6th ed. Philadelphia: Elsevier Saunders; 2011:132–156.

B.5. Would you discontinue digoxin? Why? What is its half-life?

In order to prevent digitalis intoxication after CPB, digitalis preparations are usually discontinued one half-life (1.5 to 1.7 days for digoxin, 5 to 7 days for digitoxin) before surgery. Digitalis intoxication is quite possible, especially after CPB when acid–base and electrolytes are abnormal. If a digitalis-dependent patient is in congestive heart failure (CHF), digitalis is continued until the night before surgery. However, the predisposing factors to digitalis intoxication, especially hypopotassemia and hypercalcemia, have to be prevented.

Royster RL, Butterworth J, Groban L, et al. Cardiovascular pharmacology. In: Kaplan JA, Reich DL, Savino JS, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: Elsevier Saunders; 2011:239–297.

B.6. Would you discontinue the β-blocker (metoprolol)? Why? What is its half-life? What is the role of the β-adrenergic blockers in treating congestive heart failure (CHF)?

The β-blocker (metoprolol) should be continued not only up until surgery, but probably throughout the perioperative period. In patients with unstable angina, sudden withdrawal of β-blocker may produce an exacerbation of symptoms and may precipitate acute MI. The dose of β-blocker does not need to be reduced before surgery for fear of bradycardia, hypotension, or difficulty in weaning from CPB. The half-life of oral propranolol is 3.4 to 6 hours and of metoprolol 3 hours. Both propranolol and metoprolol are metabolized in the liver. Propranolol disappears from the plasma and atria within 24 to 48 hours after discontinuing doses of 30 to 240 mg per day. Shand and Keats have shown that with a 0.5-mg dose of propranolol IV, blood levels as high as 50 ng per mL are obtained, but rapidly drop off to immeasurable levels within 5 to 10 minutes. No myocardial depression has been seen with these small intravenous doses. Current advanced cardiac life support guidelines suggest a 5-mg bolus of metoprolol at 5-minute intervals, and a 0.1 mg per kg bolus dose of propranolol divided into three equal doses at 2- to 3-minute intervals.

Reductions in HR with a β-blocker (propranolol or metoprolol) occur at lower serum levels than depression of myocardial contractility. Accordingly, as drug levels decrease after discontinuation of therapy, reductions in chronotropic response last longer than reductions in inotropy. This is an important concept in treating tachycardias in patients with significant ventricular dysfunction and CHF: a small dose is appropriate, and indicated, whereas a large dose may suppress even further the inotropic state.

Numerous studies have confirmed improvements in cardiac function, exercise capacity, and long-term survival in patients with heart failure resulting from MI, hypertrophic cardiomyopathy, or idiopathic dilated cardiomyopathy with β-antagonists. β-Antagonists may also be of benefit in patients with diastolic dysfunction, secondary to hypertension.

Potential benefits of β-adrenergic blockade in heart failure include decreased HR and normalization of β-receptor function. Slower HRs improve diastolic function by increasing the diastolic filling time and myocardial perfusion and by decreasing the myocardial oxygen consumption. β-Adrenergic receptors are downregulated in heart failure, but their response is normalized by long-term β-blockade. Partial β-agonists may provide baseline sympathetic drive but act as antagonists against excessive sympathetic stimulation.

Royster RL, Butterworth J, Groban L, et al. Cardiovascular pharmacology. In: Kaplan JA, Reich DL, Savino JS, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: Elsevier Saunders; 2011:239–297.

B.7. If the patient who is on metoprolol develops hypotension intraoperatively, how would you manage it?

The more common causes of intraoperative hypotension, such as hypovolemia, deep anesthesia, and surgical manipulation, should be corrected first. There are no specific antagonists for metoprolol. In rare instances, it is necessary to administer atropine for bradycardia or epinephrine, isoproterenol, glucagon, calcium, or digitalis to counteract the negative inotropic state associated with β-blockade. Cardiogenic hypotension is usually associated with high PAOP and low BP.

Royster RL, Butterworth J, Groban L, et al. Cardiovascular pharmacology. In: Kaplan JA, Reich DL, Savino JS, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: Elsevier Saunders; 2011:239–297.

B.8. What is nifedipine? How does it work?

Nifedipine is a calcium channel blocker. The commonly used calcium channel blockers in the United States are nifedipine, verapamil, and diltiazem hydrochloride. Five classes of compounds have been examined: phenylalkylamines, dihydropyridines, benzothiazepines, diphenylpiperazines, and diarylaminopropylamine. At present, verapamil (a phenylalkylamine); diltiazem (a benzothiazepine); nicardipine, nifedipine, isradipine, amlodipine, felodipine, nimodipine, clevidipine, (dihydropyridines); and bepridil (a diarylaminopropylamine ether) are approved for clinical use in the United States. They inhibit excitation—contraction coupling of myocardial and smooth muscle by blocking calcium influx at cellular membranes. This results in decreased myocardial contractility and vasodilation. Therefore, myocardial oxygen consumption is decreased. Calcium channel blockers are effective for the treatment of variant angina (Prinzmetal angina), angina pectoris, and possibly acute MI (see also Chapter 18, section A.11).

Although nitrates and β-adrenergic blockers are effective for angina, several of the calcium channel blockers are longer acting and may be used in the presence of chronic obstructive pulmonary disease and asthma. Calcium also plays a key role in cardiac electrical activity. The electrical activity of the sinoatrial (SA) and AV nodal cells are especially dependent on the calcium or "slow" current, whereas the remaining of the specialized conduction system is more dependent on the sodium or "fast" current. Verapamil has a more profound influence on the calcium current of the SA and AV nodes. This drug has been most useful in the treatment of supraventricular tachyarrhythmias, which are often caused by reentry through the AV node. In contrast, nifedipine has less influence on the SA node and no effect on AV conduction time. Therefore, nifedipine might be used when further suppression of AV conduction is undesirable. The relative cardiovascular effects of calcium channel blockers are shown in Table 5.1. Verapamil was found to profoundly depress the cardiovascular system during high concentrations of halothane, enflurane, or isoflurane anesthesia. However, because of a tendency for increased incidence of sinus arrest and bradycardia and more hemodynamic depression during enflurane anesthesia, Rogers et al. concluded that intravenous verapamil is better tolerated during low-dose isoflurane and halothane anesthesia than during comparable concentrations of enflurane anesthesia.

Curran MP, Robinson DM, Keating GM. Intravenous nicardipine: its use in the short-term treatment of hypertension and various other indications. *Drugs*. 2006;66(13):1755–1782.

Gradman AH, Vivas Y. New drugs for hypertension: what do they offer? *Curr Hypertens Rep*. 2006;8(5):425–432.

Royster RL, Butterworth J, Groban L, et al. Cardiovascular pharmacology. In: Kaplan JA, Reich DL, Savino JS, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: Elsevier Saunders; 2011:239-297.

Table 5.1 Relative Cardiovascular Effects of Oral Calcium Channel Blockers

	VERAPAMIL	DILTIAZEM	NIFEDIPINE
Antiarrhythmic	+++	++	–
Cardiac depression	++	+	+
Vasodilation	+	++	+++
Tachycardia	–	–	++

–, No effect; +, mild effect; ++ moderate effect; +++ marked effect.

C. Intraoperative Management

C.I. *Before Cardiopulmonary Bypass*

C.I-1. How do you monitor the patient?

- ECG—simultaneous leads V_5 and II, multiple-lead ST-segment analysis
- Arterial line for BP and arterial blood gases
- Pulmonary artery (PA) catheter—pulmonary and central venous pressures (CVP), hemodynamic parameters (cardiac output, stroke volume, systemic and pulmonary vascular resistance)
- CVP line only—if the patient has good left ventricular function and no problems are expected
- Urine output
- Temperature—esophageal (or PA) and bladder (or rectal, tympanic, or nasopharyngeal)
- Laboratory—arterial blood gases, electrolytes, hematocrit, activated coagulation time (ACT), and oxygen saturation of the mixed venous blood (Svo_2)
- Airway pressures and respiratory gases analyzer
- End-tidal CO_2 analyzer
- Pulse oximeter for plethysmography (adequacy of peripheral pulse, pulse rate) and arterial oxygenation
- Transesophageal echocardiography (TEE) if not contraindicated. Absolute contraindications are esophagectomy or esophagogastrectomy, active upper gastroesophageal bleeding, or recent surgery, oropharyngeal trauma, and presence of esophageal pathology (tracheoesophageal fistula, stricture, trauma, tumor, scleroderma, Mallory-Weiss tear, and diverticulum). However, the anticipated benefits should be weighed against potential risks in every patient, prior to deciding whether to insert a TEE probe.
- Cerebral oximeter especially for patients with high risk of postoperative neurologic outcomes, such as those undergoing hypothermic circulatory arrest.
- Bispectral index to ensure adequate level of unconsciousness and eliminate the risk of intraoperative awareness.

C.I-2. What is the Allen test?

The Allen test is used to detect the presence of adequate collateral ulnar circulation. The radial and ulnar arteries are occluded by the examiner's fingers. The patient is then asked to make a tight fist repeatedly, to empty the blood from the hand (until the palmar skin is blanched). The hand is held above the heart level to help venous drainage. If the patient is under anesthesia, the blood in the hand may be drained by a third person squeezing the hand. Then, the fist is opened slowly and put down to the heart level. Only the ulnar compression is released and the flush of the palmar skin is watched.

- Normal—less than 7 seconds (presence of adequate collateral connections between the superficial [ulnar] and deep [radial] palmar arches)

- Borderline—7 to 15 seconds
- Abnormal—greater than 15 seconds

A modified Allen test may be done with a Doppler detector or a pulse oximeter. The results of Allen test are abnormal in approximately 3% of young healthy individuals. However, Slogoff et al. studied the complications following radial artery cannulation in 1,699 cardiovascular surgical patients. They concluded that in the absence of peripheral vascular disease, Allen test is not a predictor of ischemia of the hand during or after radial artery cannulation, and that radial artery cannulation is a low-risk, high-benefit monitoring technique that deserves wide clinical use. However, in the current litigious setting and in the face of some evidence to the contrary, it is probably prudent to continue to perform Allen test and document the results. Some authorities still consider the use of Allen test as the standard of care.

Alastruey J, Parker KH, Peiro J, et al. Can the modified Allen's test always detect sufficient collateral flow in the hand? A computational study. *Comput Methods Biomech Biomed Engin.* 2006;9(6):353–361.

Barbeau GR, Arsenault F, Dugas L, et al. Evaluation of the ulnopalmar arterial arches with pulse oximetry and plethysmography: comparison with the Allen's test in 1010 patients. *Am Heart J.* 2004;147(3):489–493.

Brzezinski M, Luisetti T, London MJ. Radial artery cannulation: a comprehensive review of recent anatomic and physiologic investigations. *Anesth Analg.* 2009;109(6):1763–1781.

Cederholm I, Sorensen J, Carlsson C. Thrombosis following percutaneous radial artery cannulation. *Acta Anaesthesiol Scand.* 1986;30:227.

Hildick-Smith D. Use of the Allen's test and transradial catheterization. *J Am Coll Cardiol.* 2006;48(6):1287.

Reich DL, Mittnacht A, London M, et al. Monitoring of the heart and vascular system. In: Kaplan JA, Reich DL, Savino JS, et al., eds. *Kaplan's Cardiac Anesthesia.* 6th ed. Philadelphia: Elsevier Saunders; 2011:416–451.

Slogoff S, Keats AS, Arlund C. On the safety of radial artery cannulation. *Anesthesiology.* 1983;59:42.

C.I-3. Should you monitor temperature from multiple sites?

In many cardiac surgery centers, measurement of two or more temperatures is common in order to estimate the accurate core temperature and achieve even distribution of body heat during cooling and rewarming by extracorporeal circulation (ECC), there is uneven distribution of body heat. Esophageal, nasopharyngeal, bladder, or tympanic sites measure core temperature; the axillary and rectal sites measure peripheral temperature. Urinary bladder temperature monitoring through a urinary catheter is quite convenient and popular, and reflects a body temperature between core and periphery. During cooling and rewarming by ECC, the core temperature changes rapidly, whereas the peripheral temperature changes slowly. The opposite changes are witnessed during surface cooling or warming.

Temperatures are measured during cooling on ECC to ensure that the organs most susceptible to potential hypoperfusion, such as the brain, actually receive the protective effect of the desired hypothermia. In this regard, nasopharyngeal or tympanic membrane temperatures are the monitoring sites, although they, at times, overestimate or underestimate the actual brain temperature. During rewarming, cerebral hyperthermia is often detected, should be avoided (by maintaining a gradient of 5° C between the arterial blood and brain, with the brain having the lower temperature), and should be corrected immediately because hyperthermia increases the cerebral oxygen consumption and may exacerbate postoperative neuropsychologic dysfunction.

Several modalities can be used: fluoroscopy, echocardiography (intraoperative TEE), and by pressure tracings.

Gravlee GP, Davis RF, Karusz M, et al. *Cardiopulmonary Bypass, Principles and Practice.* Philadelphia: Lippincott Williams & Wilkins; 2000:567–568.

Grocott HP, Stafford-Smith M, Mora-Mangano CT. Cardiopulmonary bypass management and organ protection. In: Kaplan JA, Reich DL, Savino JS, et al., eds. *Kaplan's Cardiac Anesthesia.* 6th ed. Philadelphia: Elsevier Saunders; 2011:838–887.

C.I-4. How do you know that the tip of the pulmonary artery (PA) catheter is in the right ventricle (RV) or PA?

There are three main differences in the pressure tracings, as shown in Figure 5.4.

Diastolic pressure is higher in PA than in RV, because the closed pulmonary valve maintains a diastolic gradient between the PA and the RV

- PA pressure—20 to 25/5 to 10 mm Hg
- RV pressure—20 to 25/0 to 5 mm Hg

Pressure contour

- PA pressure tracing has a dicrotic notch, which is created by the closure of pulmonary valve, and the diastolic part is descending (decreasing).
- RV pressure tracing has a sharp drop and a plateau in early diastole, and the diastolic part is ascending (increasing).

Ventricular filling

- In the late diastolic phase, PA pressure is decreasing because of diastolic runoff in the pulmonary circulation, whereas the RV pressure is increasing because of ventricular filling.

C.I-5. What is normal pulmonary artery occlusion pressure (PAOP)?

- Normal—4 to 12 mm Hg
- Borderline—13 to 17 mm Hg
- Heart failure—over 18 mm Hg

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia.* 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:706–707.

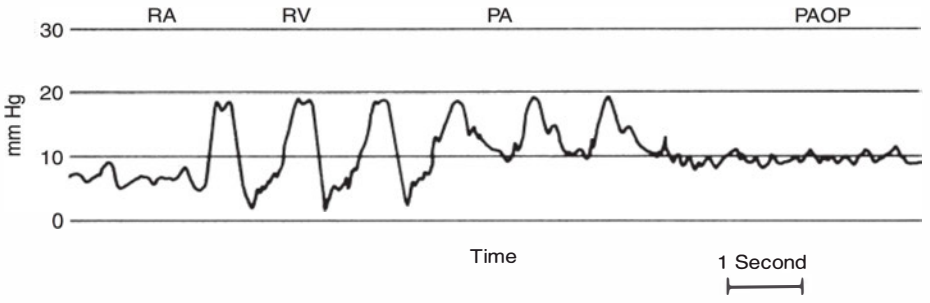


Figure 5.4 Pressure tracings of right atrium (RA), right ventricle (RV), pulmonary artery (PA), and pulmonary artery occlusion pressure (PAOP).

C.I-6. Is it necessary to monitor PA pressure for coronary artery operations?

The indication to monitor PA pressure includes the following:

Diagnostic

- Diagnosis of shock states
- Differentiation of high- versus low-pressure pulmonary edema
- Diagnosis of primary pulmonary hypertension
- Diagnosis of valvular disease, intracardiac shunts, cardiac tamponade, and pulmonary embolus
- Monitoring and management of complicated acute MI
- Assessing hemodynamic response to therapies
- Management of multiorgan system failure and/or severe burns
- Management of hemodynamic instability after cardiac surgery
- Assessment of response to treatment in patients with primary pulmonary hypertension

Therapeutic: Aspiration of air emboli

The indication to monitor PA pressure depends on the ventricular function. Patients may be divided into two categories on the basis of left ventricular function. For patients who have good left ventricular function (ejection fractions >50% and normal ventricular wall motion), the CVP is considered to correlate well with the PAOP; therefore, PA pressure monitoring may not be necessary for this group of patients. On the other hand, for patients with poor left ventricular function (ejection fractions <40% or prominent wall motion abnormalities), the CVP is not considered to correlate with the PAOP, and PA pressure monitoring is indicated. Other indications for monitoring PA pressure include the presence of pulmonary hypertension, combined coronary stenosis and valvular disease, and complex cardiac lesions.

However, results of several studies in recent past involving critically ill patients have consistently demonstrated that use of PA catheter was either associated with increased mortality and morbidity or no difference in fatal and nonfatal outcomes as compared to use of CVP alone or other noninvasive monitoring. Much debate exists regarding this topic and its unlikely that there ever will be a resolution. Nevertheless, there has been substantive reduction in the use of the PA catheter both in surgical and medical settings.

Binanay C, Califf RM, Hasselblad V, et al. Evaluation study of congestive heart failure and pulmonary artery catheterization effectiveness: the ESCAPE trial. *JAMA*. 2005;294(13):1625–1633.

Djaiani G, Karski J, Yudin M, et al. Clinical outcomes in patients undergoing elective coronary artery bypass graft surgery with and without utilization of pulmonary artery catheter-generated data. *J Cardiothorac Vasc Anesth*. 2006;20(3):307–310.

Harvey S, Harrison DA, Singer M, et al. Assessment of the clinical effectiveness of pulmonary artery catheters in management of patients in intensive care (PAC-Man): a randomised controlled trial. *Lancet*. 2005;366(9484):472–477.

Harvey S, Young D, Brampton W, et al. Pulmonary artery catheters for adult patients in intensive care. *Cochrane Database Syst Rev*. 19 2006;3:CD003408. Available at: http://emedicine.medscape.com/article/1824547-overview

Rhodes A, Cusack RJ, Newman PJ, et al. A randomised, controlled trial of the pulmonary artery catheter in critically ill patients. *Intensive Care Med*. 2002;28(3):256–264.

Richard C, Warszawski J, Anguel N, et al. Early use of the pulmonary artery catheter and outcomes in patients with shock and acute respiratory distress syndrome: a randomized controlled trial. *JAMA*. 2003;290(20):2713–2720.

Sandham JD, Hull RD, Brant RF, et al. A randomized, controlled trial of the use of pulmonary-artery catheters in high-risk surgical patients. *N Engl J Med*. 2003;348(1):5–14.

Shah MR, Hasselblad V, Stevenson LW, et al. Impact of the pulmonary artery catheter in critically ill patients: meta-analysis of randomized clinical trials. *JAMA*. 2005;294(13): 1664–1670.

Vender JS. Editorial: Pulmonary artery catheter utilization: The use, misuse, or abuse. *J Cardiothorac Vasc Anesth*. 2006;20:295–299.

Wheeler AP, Bernard GR, Thompson BT, et al. Pulmonary-artery versus central venous catheter to guide treatment of acute lung injury. *N Engl J Med*. 2006;354(21): 2213–2224.

C.I-7. What are the complications of PA catheterization?

From venopuncture sites (as for central venous pressure)

Common complications:

- Infection—sepsis
- Hematoma
- Air embolism
- Thrombosis
- Catheter shearing and embolization

Subclavian approach:

- Pneumothorax
- Hemothorax
- Hydrothorax

Internal jugular approach:

- Pneumothorax
- Neck hematoma from puncture of carotid artery
- Possible vagus nerve injury and brachial plexus injury
- Thoracic duct perforation from left-side approach

The basilar or cephalic vein approach has fewer complications, but the failure rate is higher.

From pulmonary artery catheter

Arrhythmias 1.5% to 11%, complete heart block, thromboembolism, pulmonary infarction from continuous wedging, massive hemorrhage from perforation of PA or right atrium (RA), failure to wedge, hemoptysis, intracardiac knotting, balloon rupture, endocardial thrombi, and tricuspid valve injury.

Fontes ML. *Complications of Central Venous Cannulation. Problems in Anesthesia*. Philadelphia: Lippincott Williams & Wilkins; 1998.

Murphy GS, Vender JS. Monitoring the anesthetized patient. In: Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:707–708.

Reich DL, Mittnacht A, London M, et al. Monitoring of the heart and vascular system. In: Kaplan JA, Reich DL, Savino JS, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: Elsevier Saunders; 2011:416–451.

C.I-8. What are the hemodynamic consequences of myocardial ischemia (MI)? How can you detect MI? Is PAOP a sensitive indicator of MI?

For four decades following Tennant and Wiggers' classic observation on the effects of coronary occlusion on myocardial contraction, it was believed that transient severe

ischemia caused either irreversible cardiac injury—that is, infarction—or prompt recovery. However, in the 1970s, it became clear that after a brief episode of severe ischemia, prolonged myocardial dysfunction with gradual return of contractile activity occurred, a condition termed *myocardial stunning*. Alternatively, severe chronic ischemia can result in diminished contractile performance manifested by chronic regional wall motion abnormalities (RWMA) (hibernation).

Acute myocardial ischemia affects systolic and diastolic pump function. Diastolic dysfunction usually manifests before systolic alterations in function. The immediate impact on ventricular compliance is related to the etiology of the ischemic event. Decreased myocardial oxygen supply is initially accompanied by an increase in compliance. In contrast, increased myocardial oxygen demand is associated with an immediate loss of ventricular compliance (e.g., the ventricle becomes stiffer). Therefore, the ventricle requires a higher filling pressure (end-diastolic pressure) to maintain a given stroke volume. A cascade of events occurs, which may include wall motion abnormalities, dysrhythmias, and conduction block. An 80% reduction of coronary blood flow causes akinesis (less than 10% of radial systolic thickening), whereas a 95% decrease causes dyskinesis (thinning, instead of thickening, during systole). If the ischemia becomes severe, the continuously elevated LVEDP will lead to pulmonary edema (Fig. 5.5).

Although a number of sensitive techniques are available for detection of ischemia, such as magnetic resonance spectroscopy, radio-labeled lactate determinations,

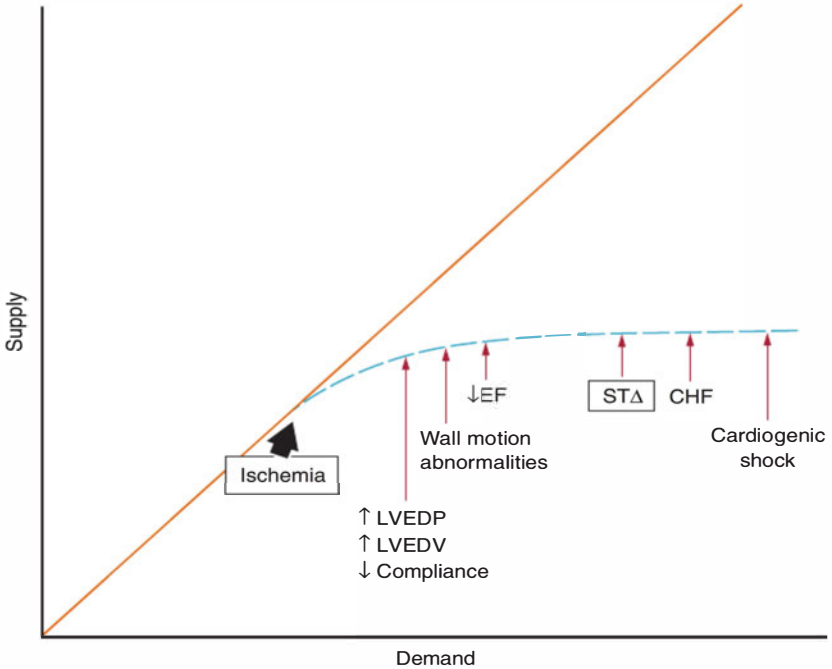


Figure 5.5 Hemodynamic consequences of myocardial ischemia. Ischemia occurs when demand exceeds supply. CHF, congestive heart failure; EF, ejection fraction; LVEDP, left ventricular end-diastolic pressure; LVEDV, left ventricular end-diastolic volume; STΔ, ST-segment changes. (From Barash PG. Monitoring myocardial oxygen balance: physiologic basis and clinical application. *ASA Refresher Courses in Anesthesiology.* 1985;13:24, with permission.)

or direct measurement of end-diastolic pressure, these are impractical. The most popular and accepted sign of ischemia is ECG ST-segment changes. The ECG criteria for ischemia are horizontal or down-sloping ST-segment depression at least 0.1 mV at 0.06 second from J-point, up-sloping ST-segment depression at least 0.2 mV at 0.08 second from J-point, and ST-segment elevation at least 0.15 mV (1 mV = 10 mm). Other ECG signs of ischemia include inverted T waves and a new onset of arrhythmias or conduction abnormalities.

RWMA, detected with two-dimensional echocardiography, have been shown to be the earliest and most sensitive sign of myocardial ischemia. RWMA are produced with just 25% decrease in coronary blood flow in the absence of ECG changes, whereas ECG signs of ischemia are apparent with a 50% decrease in coronary blood flow. During exercise, patients with CAD develop RWMA after 30 seconds, whereas ECG changes do not occur until after 90 seconds. Smith et al. found that RWMA was four times more sensitive than ECG ST-segment change in detecting intraoperative ischemia. Moreover, ST-segment changes cannot be analyzed if the patient has conduction disturbances, such as bundle-branch block or ventricular-paced rhythms. They have also found that patients experiencing persistent RWMA were more likely to have MI than those having only transient changes. No patient without a new RWMA had MI. Although TEE is the most sensitive monitor for myocardial ischemia, a recent study by Eisenberg et al. concludes that routine monitoring for myocardial ischemia with TEE or 12-lead ECG during noncardiac surgery appears to have little incremental clinical value over preoperative clinical data and two-lead ECG monitoring in identifying patients at high risk for perioperative ischemic outcome.

Measurement of PAOP has been suggested as an early and sensitive indicator of ischemia, to be used when the ECG is not diagnostic. Although acute increases in PAOP or development of V waves may reflect ischemia, the absence of a change in PAOP does not ensure the absence of ischemia. Haggmark et al. reported that the sensitivity, specificity, and predictive value (positive and negative) of PAOP abnormalities for ischemia ranged between 40% and 60%. In CABG patients, Lieberman et al. also found a low positive predictive value (24%) but a higher negative predictive value (85%); however, the PAOP was no better than CVP measurement, except in patients with moderate to severe preoperative ventricular dysfunction. Leung et al. found that 61% of TEE wall-motion abnormalities in CABG patients occurred without significant changes (>20% of control) in HR, systolic arterial pressure, or PA pressure. Only 10% of episodes were accompanied by 5 mm Hg or greater changes in PA pressure. Roizen et al. found that 11 out of 12 patients developed TEE wall-motion abnormalities when the aorta was cross-clamped above the supraceliac artery, but that PAOP remained normal (12 mm Hg) in 10 out of 12, with only 2 out of 12 having transient increases. Therefore, these studies question the value of PA catheterization and monitoring for detection of intraoperative ischemia.

Barash PG. Sequential monitoring of myocardial ischemia in the perioperative period. *ASA Annual Meeting Refresher Courses Lectures*, Park Ridge, IL: American Society of Anesthesiologists; 2002;233.

Haggmark S, Hohner P, Ostman M, et al. Comparison of hemodynamic, electrocardiographic, mechanical, and metabolic indicators of intraoperative myocardial ischemia in vascular surgical patients with coronary artery disease. *Anesthesiology*. 1989;70:19–25.

Mantha S, Ochroch EA, Roizen MF, et al. Anesthesia for vascular surgery. In Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1108–1135.

Mittnacht A, Weiner M, London M, Kaplan JA. Anesthesia for myocardial revascularization. In: Kaplan JA, Reich DL, Savino JS, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: Elsevier Saunders; 2011:522–569.

C.I-9. How would you monitor electrocardiogram (ECG)? Why V_5? If you do not have precordial leads in your ECG machine, how can you monitor the left ventricle (LV)?

Multiple-lead ECG monitoring provides the best clinically available method of detecting perioperative ischemia. Based primarily on results obtained from exercise treadmill testing, combining ECG leads II and V_5, can detect 96% of ischemic events; therefore, leads II and V_5 are the optimal leads for intraoperative myocardial ischemia. However, London et al. recently found that the standard combination of leads II and V_5 was only 80% sensitive, whereas combining leads V_4 and V_5 increased sensitivity to 90% in patients with known or suspected CAD undergoing noncardiac surgery with general anesthesia. The sensitivity increased to 96% by combining leads II, V_4, and V_5. If only one lead can be displayed, V_5 should be used because lead V_5 has the greatest sensitivity: 75% intraoperatively and 89% during exercise treadmill testing. See also Chapter 13, section C.3.

London MJ, Hollenberg M, Wong MG, et al. Intraoperative myocardial ischemia: localization by continuous 12-lead electrocardiography. *Anesthesiology.* 1988;69:232–241.

C.I-10. Discuss the principles and clinical applications of intraoperative transesophageal two-dimensional echocardiography.

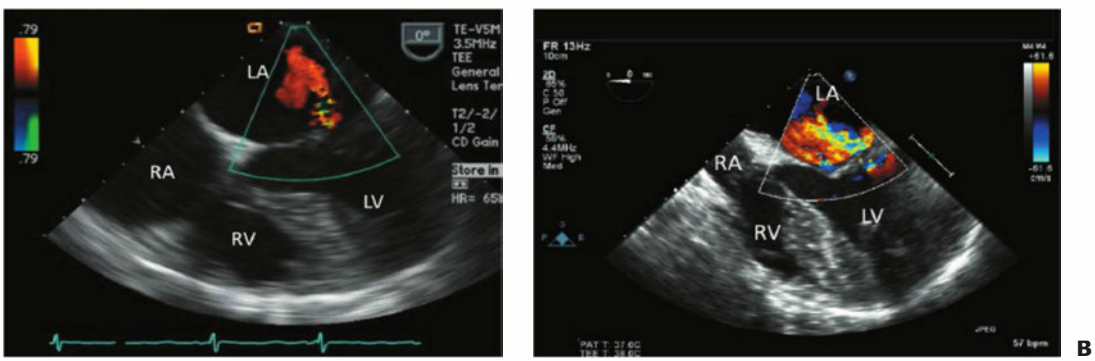
TEE is a well-established technique to visualize cardiac anatomy and function. Echocardiography is based on fundamental ultrasonic principles. Ultrasound is defined as sound above the upper threshold of human hearing (20,000 Hz). The ultrasound waves (1 to 7 MHz) are created by applying an alternating electric current of 500 to 1,500 pulses per second on a piezoelectric crystal. A short burst (pulse) of high-frequency, low-intensity sound is then emitted and directed through the human body to detect boundaries between structures of different acoustic impedance. The ultrasound wave is partially reflected at the boundary of media with different acoustic impedance, a property that is primarily determined by the slight difference in density between different tissues. The transmission of ultrasound through the heart, with detection of the returning echoes detailing the position and movement of cardiac structures, is termed *cardiac ultrasound* or *echocardiography*. Two-dimensional ultrasound reconstructs cardiac anatomy in shades of gray, from the time delay and decreased intensity of the reflected ultrasound. The ultrasound beam sweeps in an arc to give a panoramic view of the heart that results in cross-sectional images that are anatomically recognizable. M-mode ultrasound is a different technique, where the ultrasonic beam is aimed in one direction only and therefore depicts only one dimension of the target structure in an image that does not resemble cardiac structure. See also Chapter 6, section A.6.

Doppler echocardiography images blood flow by applying Doppler frequency shift analysis to echoes reflected by a moving target (red blood cells or cardiac tissue). The Doppler principle states that the frequency of the reflected ultrasound is different from the frequency of the emitted ultrasound. This shift in frequency is proportional to the speed of the moving target. Color-coded Doppler flow imaging (color flow Doppler) simultaneously presents real-time images of intracardiac blood flow and moving cardiac structures in two dimensions: continuous color maps of flow superimposed on gray-colored cross-sectional echocardiograms. Color flow Doppler permits the evaluation of valvular function and intracardiac shunts.

The clinical applications of intraoperative echocardiography are as follows:

- *Monitoring ventricular volume and function.* When left ventricular short-axis cross-section is monitored at the level of the midpapillary muscles, TEE provides the anesthesiologist with a direct, semiquantitative method to assess left ventricular preload and ejection in real time, and guide the administration of fluids and inotropes.

- *Monitoring diastolic function.* Both Doppler assessment of transmitral and transpulmonary vein flow patterns can provide important information about diastolic dysfunction that may be prevalent in as many as 50% of patients presenting for open heart surgery, namely, those with history of hypertension, aortic stenosis, and hypertrophic cardiomyopathy. It is important to note that in patients with valvular disease, a component of LV dysfunction arises from abnormal diastolic function.
- *Ischemic heart disease.* RWMA, such as hypokinesia, akinesia, and dyskinesia, are the earliest signs of myocardial ischemia (Figs. 5.2 and 5.3), as discussed in section C.I-8. Measurements of systolic wall thickening, another excellent sign of myocardial ischemia, are not reproducible because of a difficulty in delineating the epicardial border accurately in two-dimensional echocardiography. The impairment of the diastolic function can be qualitatively estimated and the filling pressures can be estimated using a combination of spectral Doppler measurements of the blood flow through the pulmonary veins and the mitral valve.
- *Valvular heart disease*
- *Air embolism.* In the left atrium, LV, and aorta, air embolism can be detected by TEE during open heart surgery. Therefore, TEE can be used to help the surgeon evacuate air bubbles from the left heart before the heart ejects blood and air into the systemic circulation.
- *Valvular regurgitation.* Valvular regurgitation can be determined intraoperatively by color Doppler echocardiography before and immediately after conservative valve repair (annuloplasty, commissurotomy) or valve replacement. The degree of valvular incompetency can be accurately measured using a combination of two-dimensional and Doppler techniques (Figs. 5.6 and 5.7), and the function of the repaired or replaced valve can be quantitatively evaluated.
- *Valvular stenosis.* Spectral Doppler echocardiography can be used intraoperatively to measure the pressure gradient across a valvular stenosis and calculate the area of the diseased valve.

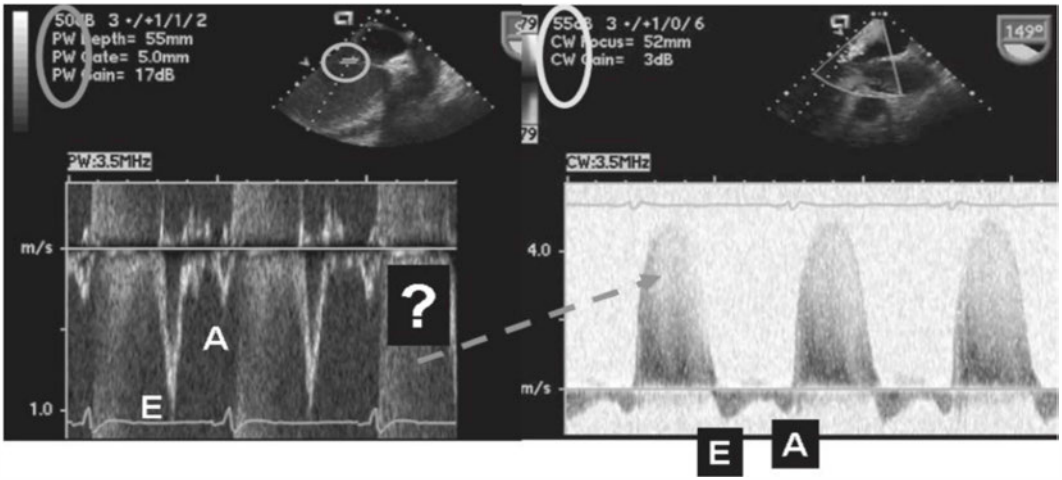


A B

Figure 5.6 Color Doppler echocardiography. **A.** Superimposed on a two-dimensional image (here, the mid-esophageal view), the relative velocities of the red blood cells from a selected area (*triangle*) are visualized. Timed to the ECG (*on the bottom of the sector image*), normal or abnormal blood flows can be viewed as they cross orifices. In this case, a small regurgitant jet originating from the mitral valve during systole is seen. The color of the jet displays velocity and direction, according to the scale, on the left side of the figure. The mitral regurgitation jet is moving upward toward the left atrium (LA), and is colored red. **B.** In this mid esophageal four chamber view of the left ventricle (LV), a systolic mitral regurgitant jet is directed inside the left atrium. RA, right atrium; RV, right ventricle.

Pulsed-wave Doppler
Site-specific (sample volume)
Aliasing limited: velocity <1.5 m/s

Continuous-wave Doppler
Cannot localize origin
Records very high velocity: 7–8 m/s



A B

Figure 5.7 Doppler mode. **A.** A typical pulsed-wave (PW) Doppler velocity consists of a spectral recording of varying intensity, depending on the acoustic density of the reflected interface (the mass of blood cells). The most dense (or brightest) portion of the spectral tracing represents the velocity of most blood cells. The velocity is recorded from a specific site (*white circle*), and the maximum velocity recorded is limited (usually <1.5 m/s). In this PW Doppler spectrum, *E* represents the diastolic early filling, and *A* the diastolic late (due to atrial contraction) velocity. During systole, there is a broad signal (*question mark*) representing systolic flow through the mitral valve (probably mitral regurgitation). However, neither the direction nor the peak velocity can be visualized. **B.** In contrast, continuous-wave (CW) Doppler records the velocities of all the red blood cells moving along the path of the sound beam. A CW Doppler recording always consists of a full spectral envelope with the outer border corresponding to the fastest moving blood cells. The site of origin of a high-velocity jet is inferred from the particular lesion that is being examined. The maximum velocity that can be recorded can be as high as 8 m/s. Here, the direction (from bottom to top, or from the left ventricle toward the left atrium) as well as the maximum systolic velocity (~ 5 m/s) can be visualized, detailing the mitral regurgitation jet.

- *Congenital heart disease*. TEE techniques allow a more aggressive approach to complex cardiac reconstructions because the surgeon has the ability to visualize the heart and evaluate adequacy of the surgical repair immediately after the operative procedure.
- *Thoracic aorta*. TEE can accurately diagnose thoracic aortic aneurysm, dissection, disruption, and atheromatosis. At the New York Presbyterian Hospital–Cornell Medical Center, we routinely use TEE for all patients to screen severe atheromatosis of the aortic arch and descending aorta. Epiaortic echocardiography is performed to examine the ascending aorta and arch if severe atheromatosis is found in the descending aorta or arch by TEE. Severe atheromatosis of thoracic aorta is an independent predictor of postoperative neurologic outcome. The atheroma is graded as follows: grade I, normal to mild intimal thickening; grade II, severe intimal thickening; grade III, atheroma protruding less than 5 mm into the lumen; grade IV, atheroma protruding greater than 5 mm; and grade V, atheroma with a mobile component (Fig. 5.8).

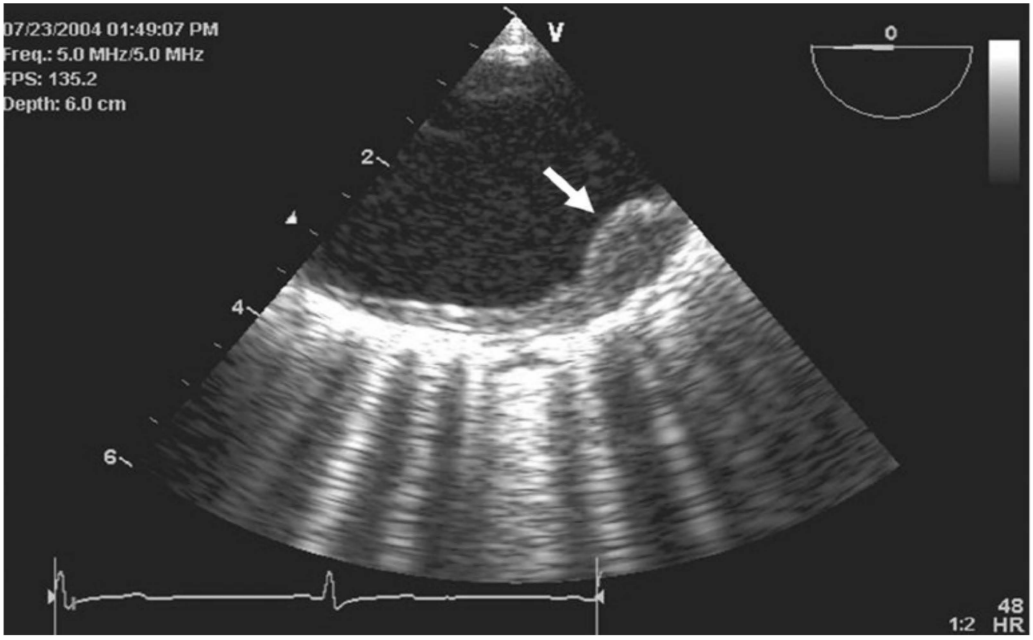


Figure 5.8 Atheromatous aortic disease. An echocardiographic picture of the short-axis view of the descending thoracic aorta is shown. The anterior aortic wall is irregularly thickened, and a large atheroma (8 mm) is present at 5 o'clock (*arrow*). This is a grade IV atheroma.

- *Cardiac tumors*. Atrial myxoma can be easily diagnosed by TEE. Preoperative and postoperative TEE with contrast can assess the presence and severity of mitral regurgitation secondary to valve damage from a ball-valve effect of the myxoma.
- *Other cardiac lesions*. Hypertrophic obstructive cardiomyopathy (HOCM) (idiopathic hypertrophic subaortic stenosis) can be identified by the combination of systolic anterior motion of the mitral valve and left ventricular outflow obstruction. Cardiac tamponade caused by a pericardial effusion or hematoma can be detected.
- *Neurosurgery*. TEE was found to be the most sensitive monitor to detect venous air embolism during neurosurgical operations in the sitting position. Patent foramen ovale and paradoxical air embolism can be detected by TEE.

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Kahn RA, Shernan SK, Konstadt SN. Intraoperative echocardiography. In: Kaplan JA, Reich DL, Lake CL, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: WB Saunders; 2011:315–382.

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Shapira Y, Vaturi M, Weisenberg DE, et al. Impact of intraoperative transesophageal echocardiography in patients undergoing valve replacement. *Ann Thor Surg*. 2004;78(2):579–583.

Troianos CA, Konstadt S. Evaluation of mitral regurgitation. *Semin Cardiothorac Vasc Anesth*. 2006;10(1):67–71.

C.I-11. How would you induce anesthesia?

Midazolam 1 to 2 mg is given as soon as the standard monitors are applied and prior to the arterial line is inserted (under local anesthesia). This is important in alleviating anxiety, which can exacerbate myocardial ischemia. A smooth induction is essential to prevent hypotension, hypertension, and tachycardia. Different techniques may be used to achieve a smooth induction. For patients with good left ventricular function, anesthesia is induced with fentanyl, 5 to 10 μg per kg; and thiopental (no longer available in the United States), 2 to 4 mg per kg; or propofol, 2 to 3 mg per kg. The patient is ventilated by mask with 100% oxygen. After administration of succinylcholine, 1 mg per kg, or pancuronium, 0.1 mg per kg, the trachea is intubated. The choice of non-depolarizing muscle relaxant varies extremely from center to among practitioners. Succinylcholine is used less frequently in cardiac surgery. If the patient has a history of hypertension or the initial systolic BP is over 150 mm Hg, fentanyl 10 μg per kg is usually required to blunt the intubation-associated hypertension and tachycardia. For patients with poor left ventricular function, potent inhalation agents such as isoflurane, sevoflurane, and desflurane should be used cautiously during induction of anesthesia because of their dose-dependent reduction in myocardial contractility and systemic arterial resistance. In lieu of the increasing incidence of delirium in the elderly postoperatively, benzodiazepines should be avoided in patients older than 70 years. Alternatively, etomidate 0.2 mg per kg may be administered for induction. However, it is more important to maintain stable hemodynamics than the choice of induction anesthetic agents. See also Chapter 10, section C.6 for other measures to prevent tachycardia and hypertension at the time of intubation.

Mittnacht A, Weiner M, London M, Kaplan JA. Anesthesia for myocardial revascularization. In: Kaplan JA, Reich DL, Savino JS, et al., eds. *Kaplan's Cardiac Anesthesia.* 6th ed. Philadelphia: Elsevier Saunders; 2011:522–569.

C.I-12. How would you maintain anesthesia?

Again, smooth anesthesia is essential to achieve a balance between myocardial oxygen demand and supply. Different agents and techniques may be used to accomplish the same goal. A combination of fentanyl (or another synthetic opioid) and isoflurane, sevofluorane, or desflurane (or propofol) is a popular choice. After the patient is intubated, a mixture of 60% air and 40% oxygen is administered to lessen the possibility of oxygen toxicity. Clearly, this ratio is subject to underlying pulmonary disease and ongoing intraoperative clinical conditions.

The depth of anesthesia must be titrated to meet the requirements of the varying intensities of surgical stimulation. Skin incision and sternal splitting are very painful. But the strongest stimulation is usually from sternal retraction with the self-retaining retractor. Fentanyl, around 5 μg (0.1 mL) per kg (or another synthetic opioid), is given right before the skin incision, before sternotomy, and intermittently throughout sugery as needed to maintain adequate analgesia. Very high doses of fentanyl or sufentanil have been successfully used for cardiac anesthesia. There has been significant changes in practice over the past decade, whereby much lower doses of narcotic are administered to facilitate early extubation. Nowadays, maintenance of anesthetic is based on administration of volatile agents and smaller opioid dosages as was the practice in the 1980s and 1990s. Vasoactive agents are also used to regulate the hemodynamics (HR, systemic arterial pressure, and filling pressures)

Mittnacht A, Weiner M, London M, Kaplan JA. Anesthesia for myocardial revascularization. In: Kaplan JA, Reich DL, Savino JS, et al., eds. *Kaplan's Cardiac Anesthesia.* 6th ed. Philadelphia: Elsevier Saunders; 2011:522–569.

C.I-13. What is the better anesthetic agent for this operation—an inhalation or intravenous agent?

Both inhalation, intravenous, and combined agents have been used successfully. Both have advantages and disadvantages. Understanding the cardiovascular effects of each anesthetic agent and careful titration of each drug will improve the balance between myocardial oxygen demand and supply. Early detection and appropriate control of the major determinants of myocardial oxygen consumption (BP, HR, PAOP) are mandatory if myocardial ischemia is to be avoided. Another consideration is the desirability of early extubation. High-dose narcotic and large doses of sedatives and muscle relaxants should be avoided if early extubation is planned.

Three large-scale outcome studies of patients undergoing CABG surgery reported that anesthetic choice did not affect incidence of perioperative morbidity and mortality. However, studies do point toward a beneficial effect of volatile agents in preconditioning the myocardium against an ischemic injury.

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Matthias R. The rocky road from bench to bedside: β-blockers and anesthetic postconditioning. *Anesthesiology.* 2009;110:451–452.

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Slogoff S, Keats AS, Dear WE, et al. Steal-prone coronary anatomy and myocardial ischemia associated with four primary anesthetic agents in humans. *Anesth Analg.* 1991;72:22–27.

Smul TM, Lange M, Redel A, et al. Desflurane-induced preconditioning against myocardial infarction is mediated by nitric oxide. *Anesthesiology.* 2006;105(4):719–725.

Tuman KJ, McCarthy RJ, Spiess BD, et al. Does choice of anesthetic agent significantly affect outcome after coronary artery surgery? *Anesthesiology.* 1989;70:189–198.

C.I-14. What are the cardiovascular effects of halothane, enflurane, isoflurane, desflurane, sevoflurane, morphine, and fentanyl?

In general, halothane, enflurane, isoflurane, desflurane, and sevoflurane produce a dose-related depression in ventricular function and vascular tonus. Halothane sensitizes the heart to catecholamine much more than enflurane, isoflurane, desflurane, and sevoflurane. Isoflurane and desflurane depress cardiac output to a lesser degree than does halothane or enflurane secondary to their greater vasodilating capacity. The HR changes least with halothane and increases most with desflurane. Isoflurane and desflurane may cause tachycardia if the inspiratory concentration is increased rapidly; the mechanism is due to increased sympathetic system outflow. Most studies suggest that halothane, enflurane, and isoflurane decrease coronary vascular resistance. Of these, isoflurane is the most potent coronary vasodilator.

All of the potent drugs decrease arterial pressure in a dose-related manner. The mechanism of BP decrease includes vasodilation, myocardial depression and decreased cardiac output, and decreased sympathetic nervous system tone. With halothane, decreased cardiac output is the predominant cause. Halothane also increases venous compliance, and in patients who have high sympathetic tone, such as those with heart failure, halothane decreases systemic vascular resistance. Enflurane causes both vasodilation and decreased myocardial contractility. With isoflurane and desflurane, a low peripheral resistance is the major cause of

hypotension. Evidence of the relatively greater myocardial depression with halothane and enflurane is the greater increase in right atrial pressure seen with these drugs than with isoflurane.

Narcotics such as morphine and fentanyl at their clinical dose have minimal cardiovascular effects. Both may cause bradycardia. Neither sensitizes the heart to catecholamine or depresses myocardial function. The cardiovascular effects of morphine depend on the dose used. Large doses of morphine sulfate have reportedly caused myocardial lactate production and reduction in coronary blood flow in animals. Sethna found that morphine sulfate, 0.25 mg per kg IV, did not produce a global myocardial ischemia in patients with CAD. High doses of morphine, 1 mg per kg, produce a significant decrease in arterial BP and systemic vascular resistance accompanied by an average 750% increase in plasma histamine. On the other hand, high doses of fentanyl, 50 μg per kg, do not produce any significant changes in BP, vascular resistance, and plasma histamine levels.

Malan TP, DiNardo JA, Isner RJ, et al. Cardiovascular effects of sevoflurane compared with those of isoflurane in volunteers. *Anesthesiology*. 1995;83:918–928.

Mittnacht A, Weiner M, London M, Kaplan JA. Anesthesia for myocardial revascularization. In: Kaplan JA, Reich DL, Savino JS, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: Elsevier Saunders; 2011:522–569.

Sethna DH, Moffitt EA, Gray RJ, et al. Cardiovascular effects of morphine in patients with coronary artery disease. *Anesth Analg*. 1982;61:109–114.

Skubas N, Lichtman AD, Sharma A, et al. Anesthesia for cardiac surgery. In: Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2006:916–919.

C.I-15. Is isoflurane dangerous for the patient with CAD?

In patients with CAD, the use of isoflurane is still controversial. Reiz et al. reported that 1% isoflurane induced coronary vasodilation that was not related to normal autoregulation and that both decreased coronary perfusion pressure (systemic hypotension), and redistribution of myocardial blood flow (coronary steal) may contribute to development of regional myocardial ischemia. Another Reiz study, using 1.5 minimum alveolar concentration (MAC) isoflurane–nitrous oxide anesthesia, concluded that isoflurane may cause coronary steal with myocardial ischemia in patients with CAD. However, Smith et al. reported that the substitution of 0.5% to 1.12% isoflurane for 85 μg per kg of fentanyl did not result in an increased incidence of myocardial ischemia, as seen by ST-segment or segmental wall-motion changes in patients with CAD. Moreover, Tarnow et al. demonstrated that 0.5% isoflurane with 50% nitrous oxide (N_2O) improved the tolerance to pacing-induced myocardial ischemia in patients with significant CAD. Two large-scale prospective outcome studies by Slogoff et al. and Tuman et al. could find no evidence that the incidence of ischemia was increased by isoflurane in patients with CAD undergoing CABG surgery. Furthermore, this finding held true even for patients with steal-prone coronary anatomy in the studies by Slogoff et al., Pulley et al., and Leung et al.

Several animal studies further confused this issue. Priebe proved that isoflurane was a myocardial depressant and a potent coronary vasodilator in the dog. Sill et al. demonstrated that high concentrations of isoflurane (1.5% and 2.5%) dilated intramyocardial arterioles rather than epicardial coronary arteries in the intact dog. Buffington et al. reported that isoflurane (1.2% to 1.5%) produced a decrease in collateral flow and a decrement in collateral zone contraction while enhancing flow in the normally perfused zone. They concluded that isoflurane was an arteriolar vasodilator and hence produced coronary steal in dogs with chronic

coronary occlusion. On the contrary, Cason et al. found that in the dog, isoflurane or halothane at 0.5% and 1.5 MAC had little effect on coronary vascular resistance, and ischemia was precipitated by tachycardia or hypotension rather than by coronary steal. Moreover, Davis and Frank demonstrated that isoflurane decreased myocardial infarct size after left anterior descending (LAD) coronary artery occlusion in dogs. In addition, Gilbert et al. reported greater coronary reserve in swine anesthetized with isoflurane versus halothane at 0.5 to 2.0 MAC. Recently, Hartman et al. demonstrated that adenosine, but not isoflurane, redistributed blood flow away from collateral-dependent myocardium in the presence of a coronary steal-prone anatomy in the chronically instrumented dog. They further found that reductions in myocardial perfusion during isoflurane anesthesia depend on systemic arterial pressure and that isoflurane did not produce coronary steal in this model of multivessel CAD. Furthermore, Cheng et al. found that neither isoflurane nor halothane as the sole anesthetic in clinical concentrations caused significant coronary vasodilation or coronary steal when the coronary perfusion pressure decreased from 55 to 30 mm Hg in a swine model of chronic coronary occlusion with collateral development.

On the basis of recent animal and recent clinical studies, we can conclude that isoflurane in clinical concentrations may be used safely in patients with CAD provided that hypotension and tachycardia are avoided.

Cheng DC, Moyers JR, Knutson RM, et al. Dose-response relationship of isoflurane and halothane versus coronary perfusion pressures. Effects on flow redistribution in a collateralized chronic swine model. *Anesthesiology*. 1992;76:113–122.

Gilbert M, Roberts SL, Blomberg RW, et al. Greater coronary reserve in swine anesthetized with isoflurane versus halothane. *Anesthesiology*. 1985;63:A15.

Hartman JC, Kampine JP, Schmeling WT, et al. Steal-prone coronary circulation in chronically instrumented dogs: isoflurane versus adenosine. *Anesthesiology*. 1991;74:744–756.

Leung JM, Goehner P, O'Kelly BF, et al. Isoflurane anesthesia and myocardial ischemia: comparative risk versus sufentanil anesthesia in patients undergoing coronary artery bypass graft surgery. *Anesthesiology*. 1991;74:838–847.

Lillehaug SL, Tinker JH. Why do "pure" vasodilators cause coronary steal when anesthetics don't (or seldom do)? *Anesth Analg*. 1991;73:681–682.

Mittnacht A, Weiner M, London M, Kaplan JA. Anesthesia for myocardial revascularization. In: Kaplan JA, Reich DL, Savino JS, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: Elsevier Saunders; 2011:522–569.

Priebe HJ. Differential effects of isoflurane on regional right and left ventricular performances and on coronary, systemic, and pulmonary hemodynamics in the dog. *Anesthesiology*. 1987;66:262–272.

Pulley DD, Kirvassilis GV, Kelermenos N, et al. Regional and global myocardial circulatory and metabolic effects of isoflurane and halothane in patients with steal-prone coronary anatomy. *Anesthesiology*. 1991;75:756–766.

Reiz S, Balfors E, Sorensen MB, et al. Isoflurane: a powerful coronary vasodilator in patients with coronary artery disease. *Anesthesiology*. 1983;59:91–97.

Reiz S, Ostman M. Regional coronary hemodynamics during isoflurane-nitrous oxide anesthesia in patients with ischemic heart disease. *Anesth Analg*. 1985;64:570–576.

Slogoff S, Keats AS, Dear WE, et al. Steal-prone coronary anatomy and myocardial ischemia associated with four primary anesthetic agents in humans. *Anesth Analg*. 1991;72:22–27.

Tarnow J, Markschies-Hornung A, Schulte-Sasseu U. Isoflurane improves the tolerance to pacing-induced myocardial ischemia. *Anesthesiology*. 1986;64:147–156.

Tuman KJ, McCarthy RJ, Spiess BD, et al. Does choice of anesthetic agent significantly affect outcome after coronary artery surgery? *Anesthesiology*. 1989;70:189–198.

C.I-16. What is the cardiovascular effect of nitrous oxide (N_2O)?

N_2O is a weak central nervous system depressant. It has been generally considered to have minimal effects on other organ systems. N_2O has significant cardiovascular effects that may be depressant or stimulatory, depending on the anesthetics with which it is combined. When high-dose fentanyl is used during coronary surgery, the effects of N_2O depend on the patient's cardiac function. Following the administration of 50% N_2O, there are no significant changes in any of the hemodynamic parameters in patients with normal left ventricular function (LVEDP <15 mm Hg). On the contrary, there is a significant decrease in cardiac index and stroke volume index in patients with left ventricular dysfunction (LVEDP >15 mm Hg). When added to other inhalation anesthetics, N_2O increases arterial pressure and systemic vascular resistance, suggesting that it has a vasoconstrictive action. N_2O increases pulmonary vascular resistance in patients with mitral stenosis and pulmonary hypertension.

The pulmonary vascular effects of N_2O are also variable. Patients with elevated PA pressure may have further increases when N_2O is added. Konstadt et al. did not corroborate these findings in patients with mitral valvular disease. A study in infants failed to show further increases of pulmonary vascular resistance with the addition of N_2O.

The contribution of N_2O to myocardial ischemia is controversial. Philbin et al. suggested that addition of N_2O to anesthesia with high-dose fentanyl (100 μg per kg followed by 1 μg/kg/min), or sufentanil (30 μg per kg followed by 0.3 μg/kg/min), can produce clinically imperceptible regional myocardial ischemia in the areas supplied by stenotic coronary arteries of dogs. However, monitoring with two-dimensional TEE did not reveal myocardial ischemia in patients with CAD when N_2O was added to low-dose fentanyl (15 μg per kg followed by 0.2 μg/kg/min), or high-dose sufentanil (20 μg per kg).

Clinically, N_2O may be used before CPB if high-dose narcotics are not used and hypotension does not occur. However, after CPB, N_2O should be avoided because of the possibility of expanding any air bubbles remaining in the coronary and cerebral circulation.

In the current clinical practices across the country, N_2O is probably used in very few centers, as the most common anesthetic scheme appears to be a balanced anesthetic with variable mixtures of oxygen in air, a potent volatile agent (amnesia) and low-dose fentanyl or sufentanil along with liberal use of vasoactive medications to regulate the hemodynamics.

Balasaraswathi K, Kumar P, Rao TLK, et al. Left ventricular end-diastolic pressure (LVEDP) as an index for nitrous oxide use during coronary artery surgery. *Anesthesiology*. 1981;55:708–709.

Cahalan MK, Prakash O, Rulf EN, et al. Addition of nitrous oxide to fentanyl anesthesia does not induce myocardial ischemia in patients with ischemic heart disease. *Anesthesiology*. 1987;67:925–929.

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Philbin DM, Fox P, Drummond G, et al. Postsystolic shortening of canine left ventricle supplied by a stenotic coronary artery when nitrous oxide is added in the presence of narcotics. *Anesthesiology*. 1985;62:166–174.

C.I-17. What kind of muscle relaxant would you use? Why?

Previously, use of pancuronium in cardiac sugery was popular. When full paralyzing doses are given in a bolus, pancuronium generally produces tachycardia and

hypertension caused by vagolytic effect and norepinephrine released from cardiac sympathetic nerves. Pancuronium is an attractive agent to avoid hypotension and bradycardia (HR <50 beats per minute) when both the systolic BP and the HR are on the thresholds of normal. Theoretically, pancuronium may increase myocardial O_2 consumption caused by tachycardia and hypertension. In practice, most patients with CAD receive β-adrenergic blocking agents, which can counteract the vagolytic effects of pancuronium. Also, the bradycardia associated with the popular narcotic anesthetic techniques can attenuate the tachycardia induced by pancuronium. Rocuronium, vecuronium, and cisatracurium have no major cardiovascular effects, but their intermediate duration of action necessitates frequent administration of the relaxant.

Mittnacht A, Weiner M, London M, Kaplan JA. Anesthesia for myocardial revascularization. In: Kaplan JA, Reich DL, Savino JS, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: Elsevier Saunders; 2011:522–569.

C.I-18. If ST-segment depression is seen during surgery, how would you treat it? What is the relation between perioperative myocardial ischemia and postoperative MI?

ST-segment depression may indicate myocardial ischemia, mostly from increased O_2 demand or decreased O_2 supply. The treatment includes the following:

- *Increase O_2 supply*. Correct hypotension (with IV phenylephrine), hypoxemia, anemia.
- *Decrease O_2 demand*. Correct hypertension, tachycardia, and increased PAOP or CVP by deepening anesthesia with a volatile agent or by using vasodilators (nicardipine or nitroglycerin) or β-blockers (metoprolol, esmolol, or labetalol). All the major determinants of decreased O_2 demand have to be considered and corrected to their normal levels.

Gerson et al. (in experimental dogs) found that elevation of ST segments induced by occlusion of the coronary artery was less prominent with halothane than with a combination of nitroprusside and propranolol. These can be explained the effects of halothane on coronary vascular reserve and the known effects of nitroprusside (reduction of myocardial blood flow to ischemic myocardium).

If there are no obvious changes in BP, HR, and pulmonary wedge pressure, nitroglycerin is indicated if coronary spasm is suspected. Nitroglycerin may be given by intravenous drip. Intravenous nicardipine or diltiazem may also be given to relieve coronary spasm.

Slogoff and Keats reported that perioperative myocardial ischemia occurred in 37% of all patients undergoing CABG. They proved that perioperative MI was almost three times as frequent in patients with ischemia (6.9%) compared with patients without ischemia (2.5%). Intraoperative tachycardia was associated with a higher incidence of myocardial ischemia and infarction. However, Knight et al. demonstrated that 42% of CABG patients had preoperative episodes of myocardial ischemia, 87% of which were clinically silent. They further found that anesthesia and surgery did not worsen the preoperative ischemic pattern. Furthermore, Slogoff and Keats in another study postulated that approximately 90% of new myocardial ischemia observed during anesthesia was the manifestation of silent ischemia observed in the patient before the operation, and only 10% was related to anesthetic management. Therefore, the relation between intraoperative ischemia and postoperative outcome is still unsolved.

It is important to note that ST-segment changes, suggestive of myocardial ischemia may be observed with alteration of the patients' position, particularly during retraction of the sternum for internal mammary harvesting. In addition to being

attentive to the ECG, addressing presence of ischemia by echocardiography and by changes in PA catheter is advised.

Gerson JI, Hickey RF, Bainton CR. Treatment of myocardial ischemia with halothane or nitroprusside-propranolol. *Anesth Analg*. 1982;61:10–14.

Hill AB, Bowley CJ, Nahrwold ML, et al. Intranasal administration of nitroglycerin. *Anesthesiology*. 1981;54:346–348.

Knight AA, Hollenberg M, London MJ, et al. Perioperative myocardial ischemia: importance of the preoperative ischemia pattern. *Anesthesiology*. 1988;68:681–688.

Mangano DT. Perioperative cardiac morbidity. *Anesthesiology*. 1990;72:153–184.

Slogoff S, Keats AS. Does perioperative myocardial ischemia lead to postoperative myocardial infarction. *Anesthesiology*. 1985;62:107–114.

Slogoff S, Keats AS. Randomized trial of anesthetic agents on outcome of coronary artery bypass operations. *Anesthesiology*. 1989;69:179–188.

C.I-19. Would you use prophylactic nitroglycerin during CABG to prevent intraoperative myocardial ischemia or perioperative MI?

No. It has been reported that prophylactic administration of nitroglycerin, 0.5 or 1.0 μg/kg/min, during fentanyl anesthesia in patients undergoing CABG did not prevent myocardial ischemia or reduce the incidence of perioperative MI.

Royster RL, Butterworth J, Groban L, et al. Cardiovascular pharmacology. In: Kaplan JA, Reich DL, Savino JS, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: Elsevier Saunders; 2011:239–297.

C.I-20. How would you correct hypertension?

$$\text{Blood pressure} = \text{blood flow} \times \text{resistance}$$

Hypertension is usually due to inadequate depth of anesthesia and/or activation of the sympathoadrenal pathways that occurs with stress/surgery. Rarely, it is due to fluid overloading. The treatment of hypertension includes the following:

- *Deepening the anesthesia*. Inhalation agents such as isoflurane and sevoflurane are more effective than narcotics because of their vasodilator effect.
- *Vasodilators*. When inhalation agents are not used.
  - Sodium nitroprusside produces more arteriolar dilation than venodilation. Dose: 10 to 100 μg per minute IV drip titration. More recently, nitroprusside's popularity has decreased and is infrequently used for acute management of perioperarive hypertension, whereas the second-generation (nicardipine) and third-generation (clevidipine) dihydroperidines calcium channel blockers have gained preference.
  - Nicardipine. Dose 0.5 μg/kg/min, titrate to effect.
  - Labetalol. Dose 5-mg increments, titrate to effect.
  - Nitroglycerin produces more venodilation than arteriolar dilation. Dose: 20 to 200 μg per minute IV drip titration, or bolus in 20-μg increments. It is important to note that this agent affects BP mainly via venodilation, which frequently will drop preload and may lower the cardiac output such that greater fluid intake may be required.

Also see Chapter 10, section C.10.

C.I-21. How would you treat hypotension?

Hypotension is usually caused by acute hypovolemia, deep anesthesia, bradycardia, or ventricular failure. The treatment options are as follows:

- Increase fluid infusion when CVP or PAOP is low (but beware of hemodilution in patients with anemia)
- Lighten the level of anesthesia or use a vasoconstrictor: phenylephrine, 0.1 mg IV increments, to correct vasodilation produced by anesthesia.
- For bradycardia, epicardial pacing may be used to increase the HR. Rarely, is atropine or other chronotropic agent used. These would include isoproterenol, ephedrine, dobutamine, epinephrine, and dopamine.
- Treat cardiac failure when PAOP is high and TEE shows global hypokinesis (poor diastolic and systolic function):
  - Avoid deep levels of anesthesia.
  - Restrict fluids.
  - Inotropes
    - $CaCl_2$ (0.5 to 1.0 g).
    - Epinephrine—2 to 8 μg per minute IV drip
    - Dobutamine or dopamine—5 to 20 μg/kg/min IV drip
    - Milrinone 0.025 mg per kg, then 0.2 to 0.5 μg/kg/min IV drip
    - Norepinephrine and/or vasopressin if peripheral vascular resistance is low.
    - Intra-aortic balloon pump (IABP)

C.I-22. What are the indications for intravenous metoprolol, labetalol, or esmolol during surgery? How much would you give? What are the relative contraindications?

Indications

- ST-segment depression associated with tachycardia; no response to deepening the level of anesthesia
- Supraventricular tachycardia
- Recurrent ventricular arrhythmias

Contraindications

- Asthma, reactive chronic obstructive pulmonary disease

Esmolol is cardioselective and appears to have little effect on bronchial or vascular tone at doses that decrease HR in humans. Esmolol is a short-acting β-blocker with an elimination half-life of 9 minutes and a pharmacologic half-life of 10 to 20 minutes. It has been used successfully in low doses in patients with asthma. Esmolol is metabolized rapidly in the blood by an esterase located in the erythrocyte cytoplasm.

Dosage

- Metoprolol, 1- to 2-mg increments every 1 to 2 minutes, total dose 5 to 10 mg.
- Esmolol, 10-mg increments up to 0.5 mg per kg followed by 50 to 300 μg/kg/min IV drip.
- Labetalol, 5-mg increments, titrate to effect. Not indicated if BP is decreased.

Royster RL, Butterworth J, Groban L, et al. Cardiovascular pharmacology. In: Kaplan JA, Reich DL, Savino JS, et al., eds. *Kaplan's Cardiac Anesthesia.* 6th ed. Philadelphia: Elsevier Saunders; 2011:239–297.

C.I-23. How would you correct increased PAOP?

It is important to consider all hemodynamics and not concentrate on one specific abnormal value. All monitored parameters should be taken into account. Increased PAOP during surgery is usually due to a light level of anesthesia or CHF. Combining the readings of PAOP and BP will produce a differential diagnosis. Occasionally, an increased PAOP with hypotension and low cardiac output is caused by HOCM, also known as idiopathic hypertrophic subaortic stenosis. HOCM can be diagnosed by TEE, which demonstrates systolic anterior motion of mitral valve and left ventricular outflow obstruction, mitral regurgitation, and usually good left ventricular contractility.

Inadequate anesthesia: Increased PAOP with hypertension

- Deepen the level of anesthesia with inhalation agents such as isoflurane, halothane, or enflurane, which also have a vasodilator effect.
- Give a vasodilator. Nitroglycerin is a better venodilator than nitroprusside.

Congestive heart failure: Increased PAOP with hypotension and low cardiac output

- Lighten the level of anesthesia.
- Use inotropes.
- Restrict fluids.
- Use arterial vasodilators to lower afterload in cases of very poor LV function and/or moderate to severe mitral insufficiency.
- Give diuretics. While an important agent for outpatient and for postoperative management of heart failure, they have extremely little to *no* role intraoperatively.

Hypertrophic obstructive cardiomyopathy

- β-Blocker and volatile agents to decrease HR and contractility
- Fluid loading to keep LV full and decrease LV outflow tract obstruction
- Increase afterload to keep LV full

Reich DL, Mittnacht A, London M, et al. Monitoring of the heart and vascular system. In: Kaplan JA, Reich DL, Savino JS, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: Elsevier Saunders; 2011:416–451.

C.I-24. What should you do during sternal splitting?

For first-time sternotomy, it is recommended that ventilation be held to protect the lungs from injury from the electric saw.

C.I-25. Would you monitor PAOP continuously? Why?

No. If the Swan-Ganz catheter balloon is inflated continuously, pulmonary infarction distal to the occlusion may ensue. Usually the gradient between PA diastolic pressure and PAOP is estimated periodically intraoperatively, and PA diastolic pressure is monitored continuously instead.

Skubas N, Lichtman AD, Sharma A, et al. Anesthesia for cardiac surgery. In: Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1073–1107.

C.I-26. Discuss autologous transfusion and blood conservation for cardiac surgery.

Autologous transfusion is the collection and reinfusion of the patient's own blood or blood components. The realization that homologous blood is responsible for transmission of AIDS, hepatitis, transfusion reaction, and autosensitization has led to increased interest in autologous transfusion and blood conservation. Most often, the easiest, safest, and most cost-effective approach for blood conservation is intraoperative normovolemic hemodilution, pharmacologic treatment, and perioperative blood salvage, while options such as preoperative autologous blood donation, preoperative use of erythropoietin, and intraoperative plasmapheresis are rarely used nowadays.

Preoperative autologous blood donation

Donations are appropriate for properly selected patients with stable CAD, stable valvular disease, and congenital heart disease. The risk of blood donation may be higher for patients with unstable angina or severe aortic stenosis; these patients are usually not considered good candidates for autologous blood donation. The patient should have a hemoglobin of greater than 11 g per dL to donate blood.

The optimal donation period begins 4 to 6 weeks before surgery, and the last donation is usually collected no later than 72 hours before surgery. Despite the potential benefits of the method, it is rarely used currently because of logistical reasons (multiple preoperative visits to the hospital, cost).

Preoperative use of erythropoietin

This is an established, efficacious but relatively expensive therapy to reduce blood transfusions. To optimize the hemoglobin response, oral or intravenous iron supplementation is recommended. The method is particularly indicated in anemic patients such as those with renal failure or patients of the Jehovah's Witness faith.

Intraoperative normovolemic hemodilution

This is the removal of blood through an arterial or venous catheter immediately after induction of anesthesia, before CPB or the administration of heparin. Depending on the patient's size and hematocrit, 500 to 1,000 mL of blood is collected into blood bags containing CPDA-1 anticoagulant and is kept at room temperature.

This blood is spared the rigors of CPB, including hemolysis, platelet destruction, and clotting factor degradation. The autologous blood is transfused after reversal of the heparin with protamine. It has been demonstrated that the effect of one unit of fresh whole blood on platelet aggregation after CPB is at least equal, if not superior, to the effect of 8 to 10 stored platelet units. However, if the patient's hematocrit is below 33% or the hemoglobin is below 11 g per dL, normovolemic hemodilution is not recommended because further decreasing the oxygen-carrying capacity may worsen myocardial ischemia. In addition, hemodilution during CPB will further decrease hematocrit to levels that require homologous blood transfusion. Normovolemic hemodilution should be performed cautiously in patients with critical left main coronary stenosis and aortic stenosis because sudden cardiac arrest has been observed during the procedure.

Pharmacologic treatment

The prophylactic use of ε-aminocaproic acid (EACA) and tranexamic acid reduces blood transfusions in cardiac surgery. The synthetic antifibrinolytics, EACA and tranexamic acid, bind to plasminogen and plasmin, thereby inhibiting binding of plasminogen at the lysine residues of fibrinogen. Effective antifibrinolysis requires a loading dose of 100 to 150 mg per kg for EACA or 10 mg per kg for tranexamic acid and a constant infusion for each at one-tenth the loading dose each hour.

Perioperative blood salvage

This is the collection and reinfusion of blood lost during and immediately after surgery. The posttransfusion survival of perioperatively salvaged red cells has been shown to be comparable to that of allogeneic red cells. At the conclusion of CPB, all blood remaining in the oxygenator and bypass circuits should be salvaged and, if needed, infused. Blood salvaged intraoperatively may be transfused directly (unwashed) or processed (washed) before infusion. Commercially available equipment exists for each option. Blood collected by intraoperative salvage represents an excellent source of red cell support. However, salvaged blood is deficient in coagulation factors and platelets.

Postoperative blood salvage is another technique of autologous blood transfusion utilizing blood lost following surgery. Blood salvaged following cardiac surgery generally is collected from mediastinal and chest drains and transfused without washing. Because usually it is defibrinated, it does not require anticoagulation before transfusion. Although dilute, the blood is sterile and contains viable red cells.

Drummond JC, Petrovich CT. Hemotherapy and hemostasis. In: Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:369–412.

Fergusson DA, Hebert PC, Mazer CD, et al. A comparison of aprotinin and lysine analogues in high-risk cardiac surgery. *N Engl J Med*. 2008;358:2319–2331.

Gravlee GP, Davis RF, Utley JR. *Cardiopulmonary Bypass, Principles and Practice*. Philadelphia: Lippincott Williams & Wilkins; 2000:536–542.

Greilich PE, Jessen ME, Satyanarayana N, et al. The effect of epsilon-aminocaproic acid and aprotinin on fibrinolysis and blood loss in patients undergoing primary, isolated coronary artery bypass surgery: a randomized, double-blind, placebo-controlled, noninferiorty study. *Anesth Analg*. 2009;109:15–24.

Lilly KJ, O'Gara PJ, Treanor PR, et al. Cardiopulmonary bypass: it's not the size, it's how you use it! Review of a comprehensive blood-conservation strategy. *J Extra Corpor Technol*. 2006;36(3):263–268.

Shander A, Moskowitz D, Rijhwani TS. The safety and efficacy of "bloodless" cardiac surgery. *Semin Cardiothorac Vasc Anesth*. 2005;9(1):53–63.

Spahn DR, Casutt M. Eliminating blood transfusions. New aspects and perspectives. *Anesthesiology*. 2000;93:245–255.

Van der Linden P. Perioperative blood conservation strategies: an update for clinicians. *Can J Anaesth*. 2006;50(6 suppl):S1–S2.

C.II. *During Cardiopulmonary Bypass*

C.II-1. What anticoagulant would you give before cardiopulmonary bypass (CPB)? How much would you give? What is its mechanism?

Heparin has been used conventionally in doses of 300 (200 to 400) units per kg of body weight, assuming an initial concentration of at least 2 to 4 units per mL of whole blood. Empirically, after 2 hours of the initial dose, subsequent doses of 1 mg per kg are given for each additional hour of bypass. Because there is marked individual variation, heparin doses are best monitored by the celite–activated coagulation time (ACT) test.

Heparin acts indirectly by means of a plasma cofactor. The heparin cofactor, or antithrombin III (AT III), is an α_2-globulin and a protease inhibitor that neutralizes several activated clotting factors: XIIa, kallikrein, XIa, IXa, Xa, IIa, and XIIIa. AT III forms irreversible complexes with thrombin (IIa) and, as a result, both proteins are inactivated. Inhibition of thrombin and factor Xa accounts for most of the anticoagulant effect of heparin. Heparin increases the rates of the thrombin–antithrombin reaction at least 1,000-fold by serving as a catalytic template to which both the inhibitor

and the protease bind. Heparin also binds to cofactor II, a glycoprotein of 65,000 Da that inactivates thrombin independently of AT III. This reaction occurs more slowly and requires higher heparin concentrates than does thrombin inhibition through the heparin–AT III complex.

Spiess BD, Horrow J, Kaplan JA. Transfusion medicine and coagulation disorders. In: Kaplan JA, Reich DL, Lake CL, et al., eds. *Kaplan's Cardiac Anesthesia.* 6th ed. Philadelphia: Elsevier Science, WB Saunders; 2011:949–991.

C.II-2. What is the half-life of heparin? How is it eliminated?

The biologic half-life of heparin varies with dosages and temperature. It has a remarkable individual variation. The average half-life is approximately 100 minutes in normothermic man for the initial doses of 300 units, increasing with higher doses and decreasing temperature. When 100, 400, or 800 units of heparin are given intravenously, the approximate half-life is 1, 2.5, and 5 hours, respectively. Heparin concentrations decline progressively at all temperatures, but the rate of decline is delayed in proportion to the hypothermia.

The primary mechanism for heparin elimination remains uncertain. Heparin appears to be cleared and degraded primarily by the reticuloendothelial system; a small amount of heparin also appears in the urine.

Spiess BD, Horrow J, Kaplan JA. Transfusion medicine and coagulation disorders. In: Kaplan JA, Reich DL, Lake CL, et al., eds. *Kaplan's Cardiac Anesthesia.* 6th ed. Philadelphia: Elsevier Science, WB Saunders; 2011:949–991.

C.II-3. How do you monitor heparin dosage? What is the activated coagulation time (ACT) test?

Heparin therapy can be assessed by the partial thromboplastin time, heparin assay, heparin–protamine titration, and the ACT test. The most convenient and practical method used to monitor heparin therapy in the operating room is the celite-ACT test. There is a very good correlation among the ACT, plasma heparin units, and thrombin time. After central venous injection of a heparin bolus, the onset of maximal ACT prolongation in the radial artery blood sample occurs within 1 minute. Previous work suggested that heparin action peaks 10 to 20 minutes after administration, but this finding probably represented an artifact from other factors prolonging the ACT such as hemodilution and hypothermia. Two milliliters of blood are put into a test tube containing celite to activate coagulation. Then, the tube is kept at 37° C (98.6° F) and clot formation is watched for ACT. The normal control value of ACT is 105 to 167 seconds. A baseline value is determined before the administration of heparin, and the test is repeated 3 to 5 minutes after heparin is given and at intervals of 30 to 60 minutes thereafter. With the dose of heparin in milligrams per kilogram on the vertical axis and ACT in seconds on the horizontal axis, a dose-response curve can be plotted. ACT values are maintained at least twice the control value and should never decrease less than 300 seconds during normothermia.

Precise determination of plasma heparin concentration can also be used. The patient's plasma is incubated with factor Xa in the presence of its inhibitor, Xai. Heparin accelerates factor Xa inhibition, and residual factor X remaining after 2 minutes is measured and converted to a heparin concentration, expressed in units per milliliter. This method has been shown to decrease the amount of heparin used compared to heparin-ACT dose-response curves. The major disadvantage of this technique is the time delay before results are available.

Gravlee GP, Davis RF, Kurusz M, et al. *Cardiopulmonary Bypass, Principles and Practice*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008:504–505.

Shore-Lesserson L. Coagulation monitoring. In: Kaplan JA, Reich DL, Lake CL, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: Elsevier Science, WB Saunders; 2011:496–521.

C.II-4. What is total CPB? What is partial bypass?

Total bypass indicates that all the venous return from superior and inferior venae cavae, and the coronary sinus is drained to the oxygenator, and no blood is pumped by the RV to the lungs. The PA and systemic pressure tracings become nonpulsatile. Partial bypass means that some of the blood return is still pumped by both RV and LV. Some venous blood is drained to the oxygenator and pumped back to the arterial side. Femoral–femoral bypass is one example of partial CPB.

Gravlee GP, Davis RF, Kurusz M, et al. *Cardiopulmonary Bypass, Principles and Practice*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008:674–675.

C.II-5. What is the purpose of venting the LV? How can it be done?

Although all the venous return is bypassed from the RV, 2% to 5% of cardiac output is draining to the LV. This represents the physiologic shunt from the bronchial, thebesian, and pleural veins. Other sources of blood flow to the left heart during CPB include aortic regurgitation from aortic insufficiency and extracardiac left-to-right shunts such as patent ductus arteriosus and Blalock-Taussig, Waterston, and Potts shunts. The left ventricular sump drain prevents overdistention of the LV, which may cause postpump heart failure. A suction needle inserted proximal to the aortic cross-clamp may serve the same purpose.

Venting of the LV can be accomplished by inserting a catheter to the following sites:

- Aortic root such as cardioplegia cannula for CABG
- Junction of the right superior pulmonary vein and the left atrium and advancing through the left atrium and mitral valve into the LV
- Apex of the LV
- PA or the left atrium only

Gravlee GP, Davis RF, Kurusz M, et al. *Cardiopulmonary Bypass, Principles and Practice*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008:89–92.

C.II-6. How many types of oxygenators are there? What are the advantages of each type?

There are two basic types of oxygenators in terms of their interface with blood.

Direct gas interface

- Disk
- Vertical screen
- Bubble

Without gas interface

- Membrane—solid or microporous
- Fluid—fluid using fluorocarbon liquid

The disk and screen oxygenators are not disposable and have proven to be somewhat difficult to clean, prepare, and resterilize.

The bubble oxygenator has the advantages of simplicity, disposability, and relatively low cost.

The disadvantages of gas interface oxygenators include the following:

- Protein denaturation
- Increased fragility of cells
- Susceptibility to hemolysis
- Denaturation of platelet membrane materials resulting in platelet aggregation, clumping
- Formation of air embolism
- Large priming volume
- Variable reservoir level resulting in potential shifts of blood volume between intracorporeal and extracorporeal circuit

The membrane oxygenator has become more popular, economical, efficient, and less traumatic to blood. Its advantages include the following:

- Less trauma to blood components
- No defoaming
- Decreased complement activation
- Independent control of oxygen and carbon dioxide exchange
- Use of air–oxygen mixture without the risk of gaseous microemboli

However, the advantage of a membrane oxygenator for a short perfusion (<2 hours) is unclear, although lower plasma hemoglobin levels are present using membrane oxygenators.

The disadvantages of membrane oxygenators include the following:

- Expense
- Potential difficulty in eliminating all bubbles during priming
- Moderately large priming volume

The major differences in changes of clotting factors between the bubble and membrane oxygenators become apparent after 4 to 6 hours of extracorporeal circulation.

Gravlee GP, Davis RF, Kurusz M, et al. *Cardiopulmonary Bypass, Principles and Practice.* 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008:47–50.

Skubas N, Lichtman AD, Sharma A, et al. Anesthesia for cardiac surgery. In: Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia.* 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1087.

Wagner JA. Oxygenator anatomy and function. *J Cardiothorac Vasc Anesth.* 1997;11:175–281.

C.II-7. What kind of priming solution would you use? How much priming solution would you use? When would you prime with blood? Why?

The usual priming solution for adults at the New York Presbyterian Hospital–Cornell Medical Center includes 1,400 mL of balanced salt solution (Normosol), 100 mL of 25% albumin, and 200 mL of 20% mannitol. The priming volumes vary with the size of the oxygenators used and the tubing volume; most oxygenators for adult patients have priming volumes of 500 to 1,000 mL. In general, blood is added to the oxygenator if the patient is markedly anemic (prepump hematocrit below 30%) or if the priming volume is large in relation to the patient's blood volume, such as in pediatric patients. In order to maintain oxygen carrying capacity, the hematocrit is kept at levels above 18% to 20%. Mannitol has long been used as an osmotic diuretic in situations where

hemolysis or diminished renal function is expected. Mannitol has been found to decrease the incidence of renal failure during hypotension by promoting osmotic diuresis and increasing renal blood flow by decreasing renal vascular resistance. Heparin, 3,000 to 10,000 units, is added to the prime depending on the size of the prime volume. This allows heparin to be distributed over the thrombogenic surfaces of the CPB circuit.

Gravlee GP, Davis RF, Kurusz M, et al. *Cardiopulmonary Bypass, Principles and Practice.* 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008:417–419, 691.

C.II-8. What are the advantages and disadvantages of hemodilution?

Advantages of hemodilution

- An increase in microcirculation due to a reduction of blood viscosity
- Improved oxygen delivery to tissues
- Decreased metabolic acidosis
- Reduced risk of hypertension
- Reduced blood demands
- Reduced incidence of hepatitis, AIDS, or reactions from blood transfusions
- Reduced postoperative blood loss
- Improved blood flow at lower perfusion pressure, especially during hypothermic perfusion

Disadvantages of hemodilution

- Decreased oxygen carrying capacity
- Postoperative extracellular fluid overload
- Possible pulmonary edema
- Increased risk of postoperative renal dysfunction
- Hypotension from decreased viscosity and peripheral resistance
- Decreased concentration of calcium, magnesium, phosphate, and zinc

Gravlee GP, Davis RF, Kurusz M, et al. *Cardiopulmonary Bypass, Principles and Practice*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008:411–422.

Habib RH, Zacharias A, Schwann TA, et al. Role of hemodilutional anemia and transfusion during cardiopulmonary bypass in renal injury after coronary revascularization: implications on operative outcomes. *Crit Care Med*. 2005;33:1749–1756.

Karkouti K, Beattie WS, David TE, et al. Hemodilution during cardiopulmonary bypass is an independent risk factor for acute renal failure in adult cardiac surgery. *J Thorac and Cardiovasc Surg*. 2005;129:391–400.

Murphy GS, Hessel EA, Groom RC, et al. Optimal perfusion during cardiopulmonary bypass: an evidence-based approach. *Anesth Analg*. 2009;108:1394–1417.

Vermeer H, Teerenstra S, Weerwind PW, et al. The effect of hemodilution during normothermic cardiac surgery on renal physiology and function: a review. *Perfusion*. 2008;23:329–340.

C.II-9. What kind of pumps do you use? Are they pulsatile or not?

There are three types of pumps available for modern CPB machines: the double-headed nonocclusive roller pump, the centrifugal blood pump, and the ventricular-type pneumatic or hydraulic pump. Only the first two types are in common use.

The roller pump is the most commonly used pump. It is driven by an afterload-independent motor. Once the pump speed is set, it will continue the forward displacement

of the same blood volume (or even air volume) even if the resistance is increased by kinking or clamping the arterial line. This will result in the rupture of connections between sections of tubing. Some centers use pressure gauges on the arterial inflow line to avoid this type of disaster.

The centrifugal pump is a kinetic pump that operates on the constrained vortex principle. Blood is driven through the pump by centrifugal forces generated by a vortex in the pump. The advantages of centrifugal pumps are as follows:

- Less trauma to blood components than the roller pump.
- Less risk of increasing arterial line pressure because blood flow decreases when line resistance is increased.
- Inflow responsiveness—if a large quantity of air is introduced into the pump, cohesive forces will no longer exist between layers of blood and pumping will stop.
- Less risk of micro-air embolism because small, low-density air bubbles are trapped in the center of the vortex.

Ventricular-type pumps, although potentially more powerful, are rather cumbersome and have not been well accepted. This type of pump is mainly used for pulsatile bypass.

The first two types of pumps are nonpulsatile. Pulsatile pumps are commercially available now. Methods available to generate pulsatile flow include an indwelling IABP, an extracorporeal balloon, ventricular-type pumps, Keele pump, Polystan pulsatile pump, modified roller pumps, and modified centrifugal pumps. Pulsatile pumps may offer advantages over continuous flow by providing diastolic runoff and stimulation of the endothelium. Improved outcomes with pulsatile pumps have been attributed to improved blood flow to vital organs and a decrease in the incidence of systemic inflammatory response syndrome. There is a decreased incidence of postoperative death in both adult and pediatric patients. Nevertheless, it has been difficult to design systems to provide sufficient pulsatility to mimic normal pulsatile circulation. In addition, the limit of pulse pressure required is also not well known. Some studies indicate that with prolonged perfusion, pulsatile flow appears to be more physiologic and superb for organ function; however, scientists are less certain that it is an important factor during short-term bypass. The differences between the two modes and a benefit for pulsatile perfusion are most clearly manifested in identifiable high-risk patient groups.

Gravlee GP, Davis RF, Kurusz M, et al. *Cardiopulmonary Bpass, Principles and Practice*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008:42–43, 284–288.

Hornick P, Taylor K. Pulsatile and nonpulsatile perfusion: the continuing controversy. *J Cardiothorac Vasc Anesth.* 1997;11:310–315.

Ji B, Undar A. An evaluation of the benefits of pulsatile versus nonpulsatile perfusion during cardiopulmonary bypass procedures in pediatric and adult cardiac patients. *ASAIO Journal.* 2006;52,4:357–361.

C.II-10. How do you monitor the patient during CPB?

Clinical monitoring

- Mean arterial pressure (MAP) should be kept between 50 and 100 mm Hg to maintain tissue perfusion. In hypertensive patients and in older patients, a higher MAP is frequently utilized—there is very little support for this in the literature.
- PA pressure should be low or zero to prevent overdistention of the LV.
- CVP should be low or zero to make sure there is no obstruction to venous return from the head (when monitored from a site proximal to the RA) or there is adequate drainage of blood to the CPB circuit (when monitored from inside the RA).

- Pump-flow rate should be adequate for tissue perfusion and oxygenation.
- Urine output should be maintained above 1 mL/kg/hour by adequate perfusion.
- ECG
- Electroencephalogram is used in patients in whom cerebral circulation problems may occur.
- Bladder and esophageal temperatures are recorded (tympanic also may be used).
- Anesthesia should be maintained at the appropriate level.
- Pupillary size should remain normal and equal.
- Transcranial Doppler and/or TEE may be used to detect aortic and cerebral embolism.
- Cerebral oximeter to maintain adequate brain oxygen saturation (>40%).

Laboratory monitoring at least once every hour

- Arterial blood gases are kept at normal range.
- Venous Po_2 should be 40 to 45 mm Hg.
- Hematocrit maintained between 20% and 30%.
- Electrolytes Na^+, K^+, ionized Ca^{2+}.
- ACT measured each hour and maintained above 400 to 480 seconds.
- Blood sugar probably should be kept below 250 mg per dL.

Gravlee GP, Davis RF, Kurusz M, et al. *Cardiopulmonary Bypass, Principles and Practice*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008:556–565.

Grocott HP, Stafford-Smith M, Mora-Mangano CT. Cardiopulmonary bypass management and organ protection. In: Kaplan JA, Reich DL, Savino JS, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: Elsevier Saunders; 2011:838–887.

Murkin JM, Adams SJ, Novick RJ, et al. Monitoring brain oxygen saturation during coronary bypass surgery: a randomized, prospective study. *Anesth Analg*. 2007;104:51–58.

Skubas NJ, Lichtman AD, Sharma A, et al. Anesthesia for cardiac surgery. In: Barash PG, Cullen BF, Stoelting RK, et al. eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1073–1107.

Yao FS, Tseng CC, Trifiletti RR, et al. Neurologic complications following cardiac surgery is associated with cerebral desaturation. *Anesth Analg*. 2000;90(45):76.

C.II-11. How much BP would you keep during CPB? Why?

Controversy continues over what constitutes adequate pressures while the patient is on bypass. The MAP is usually maintained at approximately 50 to 100 mm Hg to ensure adequate tissue perfusion. BP depends on cardiac output (pump flow) and total peripheral resistance (TPR). We believe that adequate cardiac output (pump flow) is more important for tissue perfusion than BP.

During hypothermic cardioplegia, higher systemic pressures (mean BP >70 mm Hg) are often avoided because of increased noncoronary collateral blood flow into the heart through the pericardium and pulmonary venous drainage. Such collateral flow of relatively warm blood tends to wash the colder cardioplegic solution out of the heart and decreases the hypothermic protection against myocardial ischemia.

The range of cerebrovascular autoregulation during hypothermia is controversial. Although pooled data from clinical studies indicate a lower autoregulatory threshold of 20 to 30 mm Hg in patients without cerebrovascular disease or pre-existing hypertension, other studies suggest a pressure-dependent cerebral circulation when MAP is less than 50 mm Hg. Until prospective studies clearly define the autoregulatory threshold under various clinical conditions, BP of less than 50 mm Hg should be regarded as potential physiologic trespass, which may compromise cerebral circulation. In patients with cerebrovascular disease or hypertension, higher perfusion

pressure is recommended. Gold et al. studied 248 patients randomized to either low MAP (50 to 70 mm Hg) or high MAP (80 to 100 mm Hg) during CPB and found a trend toward improvement in cardiac and neurologic outcome with higher MAP. However, MAP had no significant effect on neurologic outcome in those patients at low risk for cerebral embolization (normal to mild aortic atherosclerosis by TEE). Patients at high risk for adverse neurologic outcome (severe aortic atherosclerosis by TEE) had a significantly lower risk of worse neurologic outcome when randomized to higher MAP. More recently, widened pulse pressure was shown to be a better predictor of cerebral and renal ischemic outcomes over that of systolic or diastolic BP. Other recent data suggest that MAP during CPB is not a primary predictor of cognitive decline or stroke following cardiac surgery. However, there was an association among hypotension (<50 mm Hg) and age, and decline in spatial and figural memory. Therefore, we recommend maintenance of high MAP during CPB in patients with increased risk of neurologic outcome such as history of cerebrovascular accident or transient ischemic attack, hypertension, carotid stenosis, advanced age, and severe aortic atherosclerosis detected by TEE.

With the recent introduction of noninvasive cerebral oximetry, the frontal cortex oxygen saturation can be monitored by near-infrared spectroscopy. The technique measures the oxygen saturation of the mixed arterial and venous blood in the brain cortex. Because the volume of blood is predominantly venous, it reflects the balance between oxygen supply and demand in the brain. Our study showed good correlation between brain oxygen saturations and neurologic and cognitive outcomes. The MAP should be kept at levels enough to maintain adequate cerebral oxygen saturations (at least 70% of baseline values or >40% saturation). In a randomized controlled trial, Murkin et al. showed that in patients undergoing coronary artery bypass in whom cerebral regional oxygen saturation was monitored, profound cerebral desaturation was avoided. This led to significantly fewer incidences of major organ dysfunction and death.

Aronson S, Fontes ML. Hypertension: a new look at an old problem. *Curr Opin Anesthesiol*. 2006;19:59–64.

Fontes ML. New insights in hypertension. *ASA Refresher Course Anesthesiol*. 2006;34:43–53.

Gold JP, Charlson ME, Williams-Russo P, et al. Improvement of outcomes after coronary artery bypass: a randomized trial comparing intraoperative high versus low mean arterial pressure. *J Thorac Cardiovasc Surg*. 1995;110:1302–1311.

Gravlee GP, Davis RF, Kurusz M, et al. *Cardiopulmonary Bypass, Principles and Practice*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008:383–384.

Hartman GS, Yao F, Bruefach M, et al. Cardiopulmonary bypass at high pressure reduces stroke incidence in patients with TEE diagnosed severe aortic atheromatous disease. *Anesthesiology*. 1995;83:A141.

Murkin JM, Adams SJ, Novick RJ, et al. Monitoring brain oxygen saturation during coronary bypass surgery: a randomized, prospective study. *Anesth Analg*. 2007;104:51–58.

Murkin JM, Farrar JK, Tweed A, et al. Cerebral autoregulation and flow/metabolism coupling during cardiopulmonary bypass: the influence of $PaCO_2$. *Anesth Analg*. 1987;66:825.

Murphy GS, Hessel EA, Groom RC, et al. Optimal perfusion during cardiopulmonary bypass: an evidence-based approach. *Anesth Analg*. 2009;108:1394–1417.

Newman MF, Kramer DC, Croughwell ND, et al. Differential age effects of mean arterial pressure and rewarding cognitive dysfunction after cardiac surgery. *Anesth Analg*. 1995;81:236–242.

Yao FSF, Tseng CC, Boyd WC, et al. Cognitive dysfunction following cardiac surgery is associated with cerebral oxygen desaturation. *Anesthesiology*. 1999;91(3A):A73.

Yao FSF, Tseng CC, Boyd WC, et al. Frontal lobe dysfunction following cardiac surgery is associated with cerebral oxygen desaturation. *Ann Thorac Surg*. 1999;68:1464.

C.II-12. How would you treat hypotension during CPB?

$$\text{Mean arterial pressure (MAP)} = \text{cardiac output (CO)} \times \text{total peripheral resistance (TPR)}$$

Hypotension may be caused by low cardiac output or low peripheral resistance. First, cardiac output should be corrected by increasing the pump-flow rate. Then, if the cardiac output is adequate, peripheral resistance can be raised by giving vasopressors. We use the primarily α-adrenergic vasopressor phenylephrine in increments of 0.5 mg to raise the MAP to 50 mm Hg. In cases of more profound vasoplegia, agents such as norepinephrine and vasopressin may be required. According to Poiseuille law, low TPR usually is due to decreased viscosity or increased vascular diameter (vasodilation). During CPB using blood-free–priming solutions, total viscosity is reduced by hemodilution, although plasma viscosity is increased by hypothermia. A short period of hypotension with a MAP of approximately 30 to 40 mm Hg usually is seen in the first 5 to 10 minutes of bypass. It is due to the following causes:

- Inadequate pump flow at the beginning of bypass
- Hypoxic vasodilation from initial perfusion with blood-free primes carrying no oxygen
- Vasodilation from vasoactive materials released because of the initial reaction of the serum proteins, blood cells, and platelets with the foreign surfaces of the heart–lung machine
- Decreased plasma levels of catecholamines by hemodilution

Balasaraswathi K, Glisson SN, El-Etr AA, et al. Effect of priming volume on serum catecholamine during cardiopulmonary bypass. *Can Anaesth Soc J*. 1980;27:135–139.

Grocott HP, Stafford-Smith M, Mora-Mangano CT. Cardiopulmonary bypass management and organ protection. In: Kaplan JA, Reich DL, Savino JS, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: Elsevier Saunders; 2011:838–887.

C.II-13. How would you treat hypertension (a mean arterial pressure [MAP] of over 100 mm Hg)?

Hypertension during bypass is usually the result of inadequate depth of anesthesia, which causes increased catecholamine output and increased vascular resistance. Pump-flow rate should not be reduced to lower the pressure. Low pump flow may cause tissue hypoxia although BP is high. The most effective treatment involves administering an inhalation agent such as through the vaporizer in the heart–lung machine. Intravenous agents such as sodium thiopental, propofol, and narcotics may be used, but they are frequently not as effective and have to be supplemented with vasodilator drugs. Previously, nitroprusside and nitroglycerin were commonly used but, more recently, the IV calcium channel blockers (nicardipine and clevidipine) and beta-blockers are frequently used.

Aronson S, Dyke CM, Stierer KA, et al. The ECLIPSE trials: comparative studies of clevidipine to nitroglycerin, sodium nitroprusside, and nicardipine for acute hypertension treatment in cardiac surgery patients. *Anesth Analg*. 2008;107:1110–1121.

Singla N, Warltier DC, Gandhi SD, et al. Treatment of acute postoperative hypertension in cardiac surgery patients: an efficacy study of clevidipine assessing its postoperative antihypertensive effect in cardiac surgery-2 (ESCAPE-2), a randomized, double-blind, placebo-controlled trial. *Anesth Analg*. 2008;107(1):59–67.

C.II-14. How do you prepare an intravenous infusion of sodium nitroprusside, nicardipine, and nitroglycerin? What are the usual doses? Which do you prefer to use?

Intravenous solutions may be prepared by adding to 250 mL of 5% dextrose in water 50 mg of nitroglycerin or sodium nitroprusside, or 25 mg of nicardipine, to make a concentration of 200 μg per mL (nitroglycerin or nitroprusside) or 100 μg per mL nicardipine. The usual doses are nitroglycerin or nitroprusside 0.5 to 10 μg/kg/min, or 0.05 μg/kg/min nicardipine, determined by careful titration (Table 5.2). We prefer nitroglycerin or nicardipine infusion. Sodium nitroprusside dilates both arterial and venous smooth muscle. It is very effective in reducing both preload and afterload. It may cause cyanide and thiocyanate toxicity. Because nitroprusside dilates the intramyocardial arterioles, intracoronary steal may occur. The solution has to be covered with aluminum foil to prevent decomposition from exposure to light. Nitroglycerin primarily causes venodilation, resulting in reduction of preload and myocardial oxygen consumption. At larger doses and by the intravenous route, it has mild arteriolar dilation and reduces afterload. It has no known toxicity and does not produce intracoronary steal because it dilates epicardial arteries. It may redistribute blood flow to the subendocardium and increase collateral circulation through the myocardium. Nicardipine is a systemic and coronary arterial dilator. The afterload is decreased, while the preload is not affected. It may cause a slight increase in HR (reflex tachycardia).

Gerson JI, Allen FB, Seltzer JL, et al. Arterial and venous dilation by nitroprusside and nitroglycerin: is there a difference? *Anesth Analg.* 1982;61:256–260.

Johnson JO, Grecu L, Lawson NW. Autonomic nervous system: physiology and pharmacology. In: Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia.* 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:326–368.

C.II-15. How much pump flow would you maintain during CPB?

The pump blood flow is equivalent to cardiac output and to supply tissue oxygenation. The normal average cardiac output for adults is 70 mL/kg/min or 3.1 L/min/m^2. Because of higher metabolism, pediatric patients need higher flow rates for each unit of body weight. Usually 70% of normal cardiac output is enough to maintain tissue oxygenation. When body surface is used, both pediatric and adult patients require about the same pump flow, 2.2 to 3.1 L/min/m^2. In summary, at normothermia and normal hemoglobin levels, the pump flow is as follows:

Adults 50 to 70 mL/kg/min	or	2.2 to 3.1 L/min/m^2
Children 100 to 150 mL/kg/min	or	2.2 to 3.1 L/min/m^2

However, some perfusion teams use low-flow (40 mL/kg/min), low-pressure (approximately 40 mm Hg) bypass quite successfully. This technique has the advantages of less bleeding through intracardiac collaterals, less trauma to blood cells and platelets, and lower fluid requirements, but it also has the potential for inadequate perfusion. Clinically, low-flow and low-pressure techniques are used in conjunction with hypothermia and hemodilution. Therefore, pump blood flow should be adjusted accordingly to match the oxygen supply with demand.

Gravlee GP, Davis RF, Kurusz M, et al. *Cardiopulmonary Bypass, Principles and Practice.* 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008:555.

Grocott HP, Stafford-Smith M, Mora-Mangano CT. Cardiopulmonary bypass management and organ protection. In: Kaplan JA, Reich DL, Savino JS, et al., eds. *Kaplan's Cardiac Anesthesia.* 6th ed. Philadelphia: Elsevier Saunders; 2011:838–887.

Table 5.2 Cardiac Anesthesia Intravenous Medications[a]

DRUG	AMOUNT TO ADD	TOTAL VOLUME WITH D_5 W	CONCENTRATION	DOSAGE RANGE
Amicar (EACA)	15 g	150 mL	1 mL = 100 mg	Load: 10 g over 1/2 hr
			10 mL = 1 g	Maintenance: 1 g/hr × 5 hr
Amiodarone	450 mg	250 mL	1 mL = 1.8 mg	Initial: 150 mg over 10 min
				Followed by: 1 mg/min × 6 hr (360 mg). Then: 0.5 mg/min × 18 hr
Dexamedetomadine			1 mL = 4 μg	Load: 1.0 μg/kg over 10 min
				Maintenance: 0.2–0.7 μg/kg/hr
Diltiazem	25 mg	100 mL	1 mL = 0.25 mg	Load: 0.1–0.15 mg/kg
				Maintenance: 0.5–.25 μg/kg/min
Dobutamine	500 mg	250 mL	1 gt = 33.3 μg	5–20 μg/kg/min
			1 mL = 2 mg	
Dopamine	400 mg	250 mL (premixed)	1 gt = 26.6 μg	Renal: 1–5 μg/kg/min
			1 mL = 1.6 mg	β: 10 μg/kg/min
				α: 10–15 μg/kg/min
Epinephrine	2 mg	250 mL	8 gtt = 1 μg	2–8 μg/min
Esmolol	5 g	250 mL	1 gt = 333 μg	50–300 μg/kg/min
			1 mL = 20 mg	
Levophed	8 mg	250 mL	2 gtt = 1 μg	4–32 μg/min
Lidocaine	2 g	500 mL (premixed)	15 gtt = 1 mg	1–4 mg/min
			1 mL = 4 mg	
Milrinone	20 mg	100 mL	3 gtt = 1 μg	0.375–1 μg/kg/min
			1 mL = 200 μg	
Nicardipine	25 mg	250 mL	1 gt = 1.66 μg	Load: 5 mg/hr
				Maintenance: Increase by 2.5 mg/hr every 15 min
				Maximum amount: 15 mg/hr
Nitroprusside	50 mg	250 mL (premixed)	1 gt = 3.33 μg	1–10 μg/kg/min

(Continued)

Table 5.2 Cardiac Anesthesia Intravenous Medications[a] *(cont.)*

DRUG	AMOUNT TO ADD	TOTAL VOLUME WITH D_5 W	CONCENTRATION	DOSAGE RANGE
Nitroglycerin	50 mg	250 mL (premixed)	1 gt = 3.33 μg	10–80 μg/min
Phenylephrine	20 mg	250 mL	19 gtt = 25 μg	25–125 μg/min
Procainamide	2 g	500 mL (premixed)	15 gtt = 1 mg	Load: 500–1,000 mg (20 mg/min)
			1 mL = 4 mg	
				Dosage: 1–4 mg/min
Sodium bicarbonate	100 mEq	100 mL undiluted	1 mL = 1 mEq	1–3 mEq/kg/hr (titrate to pH)
Tranexamic acid			1 mL = 100 mg	Load: 10 mg/kg
				Maintenance: 1 mg/kg/h
Vasopressin	100 units	100 mL	1 mL = 1 unit	Initial dose: 0.04 U/min, 2.4 U/hr
				Titrate: 0.005–0.01 U/min
				(0.3–0.6 mL/hr) every 10 min to max of 0.1 U/min or 6 U/hr

[a] There are 60 guttae per milliliter (gtt/mL), therefore, gtt/min = mL/hr.
EACA, aminocaproic acid.

Kolkka R, Hilberman M. Neurological dysfunction following cardiac operation with low flow, low pressure cardiopulmonary bypass. *J Thorac Cardiovasc Surg.* 1980;79: 432–437.

C.II-16. How would you adjust the pump flow during hypothermia?

Hypothermia decreases oxygen consumption. Therefore, the pump flow may be decreased proportionally if the blood oxygen content does not change. The oxygen consumption at different body temperatures is listed in the following text:

Temperature (° C)	37	32	30	28	25	20	10
O_2 consumption (%)	100	60	50	40	25–30	20	10

Because the O_2 consumption at 30° C (86° F) is half of that at 37° C (98.6° F), the required pump flow at 30° C (86° F) is 50% of the flow at 37° C (98.6° F) (50° to 70 mL/kg/min). Therefore, a pump flow of 25 to 35 mL/kg/min is adequate for adults at 30° C (86° F) if there is no hemodilution. During profound hypothermia (10° to 20° C [50° to 68° F]), the patients usually can tolerate total circulatory arrest without pump support for approximately 60 to 90 minutes. The decrease in metabolism during hypothermia is not a linear process. From 37° to 30° C (98.6° to 86° F), the metabolism decreases approximately 7% by each degree centigrade. Below 30° C

(86° F), the rate of metabolism decrease slows down. Usually, every 7° to 8° C (44.4° to 46.4° F) decrease in temperature reduces oxygen consumption by 50%. Clinically, it has been demonstrated that pump flows as low as 30 mL/kg/min or 1.2 L/min/m^2 will not compromise whole-body oxygen delivery when moderate systemic hypothermia is employed.

C.II-17. How would you adjust the pump flow during hemodilution?

$$\text{Oxygen delivery} = \text{cardiac output} \times \text{arterial oxygen content}$$
$$\text{Arterial oxygen content} = 1.34 \times \text{hemoglobin} \times O_2 \text{ saturation} + (0.003 \times Pao_2)$$

Hemodilution reduces hemoglobin concentration and hence decreases oxygen content. In order to deliver the same amount of oxygen, the pump flow has to be increased accordingly during hemodilution. For example, if the hematocrit is diluted from 40% to 20% during CPB, the pump flow has to be doubled (increased by a factor of 40/20 = 2). Clinically, both hypothermia and hemodilution are applied simultaneously so that the adjustment has to be done at the same time. For example, the pump flow for adults at a temperature of 30° C (86° F) and a hematocrit of 25% will be as follows:

$$50 \text{ to } 70 \text{ mL/kg/min} \times 50\% \times 40/25 = 40 \text{ to } 56 \text{ mL/kg/min}$$

C.II-18. What are the advantages of hypothermia? Does hypothermia offer neuroprotection?

Hypothermia decreases oxygen consumption and helps to preserve the function of tissues during a hypoxic or ischemic insult. Pump flow may be decreased during CPB with hypothermia.

Hypothermia has been shown to confer significant protection in the setting of transient, but not permanent, ischemia. The mechanism is unclear. The reduction in cerebral metabolic rate is believed to be less important when compared with the effect of hypothermia on the release of excitatory neurotransmitters, catecholamines, or other mediators of cellular injury. It is for this reason that mild hypothermia (33° to 35° C [91.4° to 95° F]) provides significant neuroprotection.

The effect of hypothermia during CPB on postoperative cognitive or neurologic function remains controversial. Animal models show profound reduction in infarct size and release of excitatory amino acid with minimal levels of hypothermia. However, clinical studies comparing normothermic and moderately hypothermic CPB have yielded conflicting results and did not produce evidence of protection from cognitive decline. This may relate to differences in defining normothermia. Many groups allow temperature to drift downward during normothermic CPB, with temperature decreasing to below 34° C (93.2° F). McLean, in a recent study of this type, showed no difference in cognitive or neurologic outcome between warm and moderately hypothermic groups. In actuality, this is a study of mild versus moderate hypothermia confirming the experimental animal data that as little as 2° to 3° C (35.6° to 37.4° F) of hypothermia markedly reduces excitatory amino acid release and neurologic injury compared to normothermia. The single large study comparing true normothermia with hypothermia during CPB showed a significantly greater incidence of focal neurologic injury in the warm group, supporting the beneficial role of hypothermia in neuroprotection. In addition, recent data showed that minimum CPB temperatures greater than 35° C (95° F) increased the incidence of perioperative stroke approximately fourfold (4.5% vs. 1.2%).

In this context, the avoidance of cerebral hyperthermia deserves comment. Hyperthermia as little as a 2° C (35.6° F) increase in temperature significantly worsens neurologic outcomes. It has been demonstrated in a rat model, that following

10 minutes of ischemia during which temperature was increased from 35° to 39° C (95° to 102.2° F), the percentage of damaged neurons increased from 15% to 80%. This is clinically relevant because cerebral temperatures above 39° C (102.2° F) have been documented in patients during rewarming, a period when cerebral embolic risk is greatest. Therefore, hyperthermia should be carefully monitored and avoided. Grigore et al. found greater neuropsychological dysfunction in patients randomized to a faster rather than slower rewarming rate in the setting of CABG surgery. Of note, the patients rewarmed at a faster rate were also exposed to higher peak temperatures and a higher mean temperature of greater than 37° C than patients rewarmed slower with lower peak temperatures.

Gravlee GP, Davis RF, Kurusz M, et al. *Cardiopulmonary Bypass, Principles and Practice*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008:383–388.

Grigore AM, Grocott HP, Mathew JP, et al. The rewarming rate and increased peak temperature alter neurocognitive outcome after cardiac surgery. *Anesth Analg*. 2002;94:4–10.

Grocott HP, Stafford-Smith M, Mora-Mangano CT. Cardiopulmonary bypass management and organ protection. In: Kaplan JA, Reich DL, Savino JS, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: Elsevier Saunders; 2011:838–887.

McLean RF, Wong BI. Normothermic versus hypothermic cardiopulmonary bypass: central nervous system outcomes. *J Cardiothorac Vasc Anesth*. 1996;10:45–53.

Murphy GS, Hessel EA, Groom RC, et al. Optimal perfusion during cardiopulmonary bypass: an evidence-based approach. *Anesth Analg*. 2009;108:1394–1417.

Nathan HJ, Rodriguez R, Wozny D, et al. Neuroprotective effect of mild hypothermia in patients undergoing coronary artery surgery with cardiopulmonary bypass: five year followup of a randomized trial. *J Thorac Cardiovasc Surg*. 2007;133:1206–1211.

Rees K, Beranek-Stanley M, Burke M, et al. Hypothermia to reduce neurological damage following coronary artery bypass surgery. *Cochrane Database Syst Rev*. 2006; CD002138.

Shann KG, Likosky DS, Murkin JM, et al. An evidence-based review of the practice of cardiopulmonary bypass in adults: a focus on neurologic injury, glycemic control, hemodilution, and the inflammatory response. *J Thorac Cardiovasc Surg*. 2006;132:283–290.

Yao FSF, Barbut D, Leon FJ, et al. Cerebral hyperthermia during cardiopulmonary bypass rewarming in patients undergoing cardiac surgery. *Anesthesiology*. 1998;89(3A):A238.

C.II-19. How does blood viscosity change during hypothermia and hemodilution?

Blood viscosity varies inversely with temperature; a 2% increase occurs for every 1° C (1.8° F) decrease in temperature. At a hematocrit of 40%, a decrease in temperature from 37° to 27° C (98.6° to 80.6° F) increases viscosity by approximately 25%. Hemodilution with balanced salt solution will decrease blood viscosity. Decreasing the hematocrit from 40% to 20% at 27° C (80.6° F) decreases viscosity by approximately 40%. It has been recommended that the hematocrit be adjusted to the same numerical value as the core body temperature in degree centigrade if blood viscosity is to be kept approximately constant. For example, normal viscosity at 37° C (98.6° F) with hematocrit of 40% approximates that seen at 25° C (77° F) with hematocrit of 25%.

Gravlee GP, Davis RF, Kurusz M, et al. *Cardiopulmonary Bypass, Principles and Practice*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008:413.

C.II-20. What are the main causes of death associated with accidental hypothermia?

Ventricular fibrillation and asystole are the major rhythm disturbances leading to cardiac arrest during hypothermia. In humans externally cooled for cardiac surgery, ventricular fibrillation generally occurs at 23° C (73° F) and asystole at 20° C (68° F). However, asystole and ventricular fibrillation have been reported at 21° to 28° C (69.8° to 82.4° F). Respiratory arrest usually accompanies cardiac arrest during accidental hypothermia.

Gravlee GP, Davis RF, Kurusz M, et al. *Cardiopulmonary Bypass, Principles and Practice.* 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008:676–677.

Southwick FS, Dalglish PH. Recovery after prolonged asystolic cardiac arrest in profound hypothermia. *JAMA.* 1980;243:1250–1253.

C.II-21. Would you give anesthesia during CPB? Why?

Anesthesia is maintained with intermittent administration of intravenous propofol, benzodiazepines, narcotic, and/or inhalation agents through the pump oxygenator to achieve unconsciousness and analgesia, to control BP, and to prevent shivering. Intravenous agents are diluted by the priming solution during CPB. Meanwhile, hypothermia itself produces anesthesia and prolongs the action duration of intravenous agents by decreasing hepatic metabolism and urinary excretion.

Gravlee GP, Davis RF, Kurusz M, et al. *Cardiopulmonary Bypass, Principles and Practice*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008:247.

Nussmeier NA, Fish KJ. Neuropsychological dysfunction after cardiopulmonary bypass: a comparison of two institutions. *J Cardiothorac Vasc Anesth.* 1991;5:584–588.

Zaiden JR, Klochany A, Martin WM, et al. Effect of thiopental on neurologic outcome following coronary artery bypass grafting. *Anesthesiology.* 1991;74:406–411.

C.II-22. Would you give muscle relaxants during CPB? How is the action of muscle relaxant affected during CPB?

Yes. Muscle relaxants are given to prevent diaphragmatic movement that interferes with surgery and to prevent shivering during hypothermia. Shivering may increase oxygen consumption to as high as 486% of normal. The effect of a muscle relaxant is altered by both hypothermia and hemodilution. The plasma concentration of muscle relaxants is diluted by the priming solution. Therefore, more relaxant is required to maintain the same degree of relaxation. Hypothermia was originally reported to decrease the effect of nondepolarizing relaxants, because decreased cholinesterase enzyme activity during hypothermia resulted in more acetylcholine accumulation to compete with the nondepolarizing relaxant. Contrary to the earlier reports, it is now established that atracurium, vecuronium, or pancuronium is needed to maintain muscle relaxation during hypothermia because hypothermia reduces renal and biliary excretions. Hypothermia does prolong the onset of paralysis. Moreover, hypothermic CPB per se facilitates neuromuscular transmission at the electrochemical level, yet compromises mechanical contractility. The duration of action of rocuronium is prolonged by hypothermic CPB.

Modifications of partial neuromuscular blockade by hypothermic bypass are the result of muscle relaxation enhancing or interfering with the impact of hypothermia on normal neuromuscular transmission. The best way to monitor muscle relaxation is by using a peripheral nerve stimulator.

Buzello W, Pollmaecher T, Schluermann D, et al. The influence of hypothermia cardiopulmonary bypass on neuromuscular transmission in the absence of muscle relaxants. *Anesthesiology*. 1986;4:279–281.

Buzello W, Schluermann D, Schindler M, et al. Hyperthermic cardiopulmonary bypass and neuromuscular blockade by pancuronium and vecuronium. *Anesthesiology*. 1985;62:201–204.

Gravlee GP, Davis RF, Kurusz M, et al. *Cardiopulmonary Bypass, Principles and Practice*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008:227–247.

Grogan K, Nyhan D, Berkowitz DE. Pharmacology of anesthetic drugs. In: Kaplan JA, Reich DL, Lake CL, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: Elsevier Science, WB Saunders; 2006:202.

Smeulers NJ, Wierda JM, Van den Broek L, et al. Effects of hypothermic cardiopulmonary bypass on the pharmacodynamics of rocuronium. *J Cardiothorac Vasc Anesth*. 1995;9:700–705.

C.II-23. How do you know the patient is well perfused during CPB?

If the perfusion pressure is maintained between 50 mm Hg and 100 mm Hg, and the pump-flow rate is adequately maintained according to the degree of hypothermia and hemodilution, there should be adequate urine output, greater than 1 mL/kg/hour, no metabolic acidosis, and normal mixed venous oxygen tension of 40 to 45 mm Hg. However, cerebral perfusion is not routinely monitored and the autoregulation range of BP may be higher than the normal range in the elder and high-risk patients. Cerebral oximetry should be used for patients with increased risk for neurologic and cognitive outcomes. It is recommended to keep cerebral oxygen saturation over 40%.

Gravlee GP, Davis RF, Kurusz M, et al. *Cardiopulmonary Bypass, Principles and Practice*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008:160–162.

Grocott HP, Stafford-Smith M, Mora-Mangano CT. Cardiopulmonary bypass management and organ protection. In: Kaplan JA, Reich DL, Savino JS, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: Elsevier Saunders; 2011:838–887.

Murphy GS, Hessel EA, Groom RC, et al. Optimal perfusion during cardiopulmonary bypass: an evidence-based approach. *Anesth Analg*. 2009;108:1394–1417.

Yao FSF, Tseng CC, Boyd WC, et al. Neurological complications following cardiac surgery is associated with cerebral oxygen desaturation. *Anesth Analg*. 2000;90:76.

Yao FSF, Tseng CA, Ho CA, et al. Cerebral oxygen desaturation is associated with early postoperative neuropsychological dysfunction in patients undergoing cardiac surgery. *Cardiothorac Vasc Anesth*. 2004;18:552–558.

C.II-24. How much gas flow would you use for the oxygenator? What kind of gas would you use? Why?

Normal alveolar ventilation is 4 L per minute and pulmonary circulation is 5 L per minute. The $\dot{V}/\dot{Q}$ ratio is 0.8. The oxygenator is not as efficient as human lungs. We usually start with 2 L of gas for each liter of pump-flow rate, and then adjust the gas-flow rate according to blood $Paco_2$ and Pao_2. The gas flow may be decreased if the $Paco_2$ is low and the Pao_2 is too high. The ratio may be increased if the $Paco_2$ is over 40 mm Hg or the Pao_2 is under 100 mm Hg. In the past, we used a mixture of 99% oxygen and 1% carbon dioxide for the bubble oxygenator. Because of low CO_2 production during hypothermia, high CO_2 elimination from high gas flow, and high CO_2 diffusion capacity, 1% CO_2, was added to oxygen to prevent severe hypocapnia. Because the routine use of membrane oxygenators oxygen–air mixtures instead of

100% oxygen have been used. In a bubble oxygenator, bubbles containing nitrogen may be slowly absorbed into the systemic circulation, increasing the risk of gaseous microemboli. In a membrane oxygenator, this risk does not exist. Meanwhile, air–oxygen mixtures allow better control of oxygen tension during CPB. Because we use alpha-stat regulation for acid–base management, it is not necessary to add CO_2 to the ventilating gas during hypothermia to elevate $Paco_2$ and decrease the pH.

Gravlee GP, Davis RF, Kurusz M, et al. *Cardiopulmonary Bypass, Principles and Practice*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008:157–164.

C.II-25. What are the disadvantages of hypocapnia during CPB?

- Cerebral blood flow decreases approximately 2% to 4% for each mm Hg decrease in $Paco_2$ when $Paco_2$ is in the range of 20 mm Hg to 60 mm Hg due to cerebral vasoconstriction. Cerebral oxygen saturation decreases approximately 1% for each mm Hg decrease in $Paco_2$.
- Respiratory alkalosis shifts the oxygen dissociation curve to the left, which increases the O_2 affinity to hemoglobin and decreases the release of O_2 to the tissues.
- Hypokalemia occurs because alkalosis shifts the potassium intracellularly.
- Alkalosis decreases ionized calcium.

Gravlee GP, Davis RF, Kurusz M, et al. *Cardiopulmonary Bypass, Principles and Practice*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008:157–164.

Smith AL, Wollman H. Cerebral blood flow and metabolism: effects of anesthetic drugs and techniques. *Anesthesiology*. 1972;36:378–400.

Yao FSF, Tseng CC, Yu J, et al. Relationship between E TCO_2 and cerebral oxygen saturation. *Anesthesiology*. 2000;93(3A):A320.

C.II-26. The arterial blood gases and electrolytes during CPB are as follows: pH, 7.36; $Paco_2$, 42 mm Hg; Pao_2, 449 mm Hg; CO_2 content, 24 mEq per L; Na, 128 mEq per L; K, 5.8 mEq per L; and Hct, 20%. The patient's temperature is 27° C (80.6° F). At what temperature are blood gases measured? How would you correct the blood gases according to patient's body temperature? Would you treat the arterial blood gases at 37° C (98.6° F) or at patient's body temperature?

Blood gases are measured at a constant temperature of 37° C (98.6° F). They may be corrected according to body temperature. Each degree centigrade below 37° C (98.6° F) increases blood pH by 0.015. If pH is 7.40 at 37° C (98.6° F) in vitro, in vivo pH will be 7.55 at 27° C (80.6° F) body temperature ($7.40 + 0.015 \times [37 - 27] = 7.55$). The pH increases at lower temperatures, because of increased Pka and decreased CO_2 tension from increased CO_2 blood solubility during hypothermia. In vivo Pao_2 is decreased because of increased oxygen solubility during hypothermia. At the New York Presbyterian Hospital–Cornell Medical Center, we measure blood gases at 37° C (98.6° F) and interpret at 37° C (98.6° F) without correcting them to body temperature. The normal values of blood gases at 37° C (98.6° F) are as follows: pH, 7.40 ± 0.05; $Paco_2$, 40 ± 5; and Pao_2, 95 ± 5. During hypothermia, the normal values of blood gases are not the same as those at 37° C (98.6° F). The same blood specimen has different Po_2 values when measured at different temperatures. Yet, the oxygen content remains unchanged. It is easier to calculate the oxygen content at 37° C (98.6° F) than at other temperatures where oxygen dissociation curves are shifted.

Optimal management of pH and $Paco_2$ for patients undergoing hypothermic CPB remains controversial. The two strategies for interpreting blood gases are the pH-stat (temperature-corrected) method and the alpha-stat (temperature-uncorrected) method. The pH-stat strategy aims at keeping constant arterial pH at 7.40 and $Paco_2$ at 40 mm Hg at any given temperature. A $Paco_2$ of 60 mm Hg analyzed at 37° C (98.6° F) would be equivalent to a $Paco_2$ of 40 mm Hg if "corrected" for a body temperature of 27° C (80.6° F). The alpha-stat strategy aims at keeping a constant ratio of $[OH^-] : [H^+]$ at approximately 16 : 1. This is based on the premise that the pH of blood is regulated to keep the state of dissociation of imidazole moiety (i.e., the alpha of imidazole) constant. Histidine, which contains the imidazole moiety, is an integral part of the active site of many enzyme systems. The function of enzyme systems has been shown to be optimal when the ratio of $[OH^-] : [H^+]$ is approximately 16 : 1. This ratio represents different pH values at different temperatures.

The differences between pH-stat and alpha-stat strategies are listed in Table 5.3. With the pH-stat strategy, the blood gas values are corrected to the patient's temperature; the patient is treated as if he were a hibernating animal. With the alpha-stat strategy, the blood gas values are not corrected regardless of the patient's actual temperature; the patient is treated as if he were a poikilotherm. Studies indicate that myocardial function is better preserved when the alpha-stat strategy is employed. Moreover, maintenance of cerebral blood flow autoregulation appears to remain intact with alpha-stat management, whereas flow becomes pressure dependent with pH-stat management. Alpha-stat blood gas management preserves cerebral blood flow-metabolism coupling such that hypothermic-induced decreases in metabolic rate are accompanied by proportionate decreases in cerebral blood flow. Therefore, most medical centers use alpha-stat management of blood gases during hypothermic CPB. However, Bashein et al. found no difference in neuropsychologic outcome between patients randomized to alpha-stat and those randomized to pH-stat management.

However, more recent studies have shown less decline in cognitive performance when alpha-stat management is used, especially in cases with prolonged CPB times. These data may support an embolic threshold above which recognizable neurologic injury occurs.

During deep hypothermic circulatory arrest, both animal and clinical studies have shown that pH-stat is associated with better neurologic outcome probably because of increased cerebral blood flow, which provides better brain cooling and greater cellular oxygen availability. In summary, most recent outcome studies support the utilization of alpha-stat for adult CPB and pH-stat for children under deep hypothermic circulatory arrest.

Bashein G, Townes BD, Nessly ML, et al. A randomized study of carbon dioxide management during hypothermic cardiopulmonary bypass. *Anesthesiology.* 1990;72:7–15.

Dahlbacka S, Heikkinen J, Kaakinen T, et al. pH-stat versus alpha-stat acid-base management strategy during hypothermic circulatory arrest combined with embolic brain injury. *Ann Thorac Surg.* 2005;79(4):1316–1325.

Gravlee GP, Davis RF, Kurusz M, et al. *Cardiopulmonary Bypass, Principles and Practice.* 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008:157–164.

Jonas RA. Hypothermia, circulatory arrest and the paediatric brain. *J Cardiothorac Vasc Anesth.* 1996;10:66–74.

Murkin JM. Central nervous system dysfunction after cardiopulmonary bypass. In: Kaplan JA, Reich DL, Lake CL, et al., eds. *Kaplan's Cardiac Anesthesia.* 6th ed. Philadelphia: Elsevier Science, WB Saunders; 2011:1061-1085.

Murkin JM, Farrar JK, Tweed WA, et al. Cerebral autoregulation and flow/metabolism coupling during cardiopulmonary bypass: the influence of $PaCO_2$. *Anesth Analg.* 1987;66:825–832.

Murkin JM, Martzke JS, Buchan AM, et al. A randomized study of the influence of perfusion technique and pH management strategy in 316 patients undergoing coronary artery bypass surgery. II. Neurologic and cognitive outcomes. *J Thorac Cardiovasc Surg.* 1995;110:349–362.

Table 5.3 Different Hypothermic Acid–Base Regulatory Strategies

STRATEGY	AIM	TOTAL CO_2 CONTENT	pH AND $Paco_2$ MAINTENANCE	INTRACELLULAR STATE	α-IMIDAZOLE AND BUFFERING	ENZYME STRUCTURE AND FUNCTION	CEREBRAL BLOOD FLOW AND COUPLING	EFFECT ON ISCHEMIC TISSUE
pH-stat	Constant pH	Increases	Normal corrected values	Acidotic (excess H^+)	Excess (+) charge	Altered and activity decreased	Flow close to normothermic	? Lessens hypothermic protection
					Buffering decreased		? Flow and metabolism uncoupled	
Alpha-stat	Constant OH^-/H^+	Constant	Normal uncorrected values	Neutral ($H^- = OH^-$)	Constant net charge	Normal and activity maximal	Flow decreases (appropriate)	? Allows full hypothermic protection
					Buffering constant		? Flow and metabolism coupled	

(From Tinker JH, ed. *Cardiopulmonary Bypass: Current Concepts and Controversies*. Philadelphia: JB Lippincott; 1989:16, with permission.)

Newmann MF, Kirschner JL, Phillips-Bute B, et al. Longitudinal assessment of neurocognitive function after coronary artery bypass surgery. *N Engl J Med.* 2001; 344:395–402.

O'Dwyer C, Prough DS, Johnston WE. Determinants of cerebral perfusion during cardiopulmonary bypass. *J Cardiothorac Vasc Anesth.* 1996;10:54–65.

Pokela M, Dahlbacka S, Biancari F, et al. pH-stat versus alpha-stat perfusion strategy during experimental hypothermic circulatory arrest: a microdialysis study. *Ann Thorac Surg.* 2003;76(4):1215–1226.

Prough DS, Stump DA, Roy RC, et al. Response of cerebral blood flow to phenylephrine infusion during hypothermic cardiopulmonary bypass: influence of $PaCO_2$. *Anesthesiology.* 1986;64:576–581.

Shann KG, Likosky DS, Murkin JM, et al. An evidence-based review of the practice of cardiopulmonary bypass in adults: a focus on neurologic injury, glycemic control, hemodilution, and the inflammatory response. *J Thorac and Cardiovasc Surg.* 2006;132:283–290.

Tallman RD. Acid-base regulation, alpha-stat, and the emperor's new clothes. *J Cardiothorac Vasc Anesth.* 1997;11:282–288.

C.II-27. If the blood level of the venous reservoir is low, what would you replace it with? Blood or balanced salt solution?

We try to maintain a hematocrit of at least 18% to 20% during hemodilution. If the hematocrit decreases below 18% to 20%, blood is added to the CPB circuit. If the hematocrit is above 20%, a balanced salt solution (Normosol) is added to the oxygenator. However, hematocrit values in the range of 15% to 18% appear to be well tolerated clinically. When cerebral oxygen saturation (rSo_2) is less than 40%, we use packed red cells to improve oxygen-carrying capacity. When rSo_2 is over 40%, it means the patient has acceptable cerebral oxygenation although hematocrit is below 18%.

Gravlee GP, Davis RF, Kurusz M, et al. *Cardiopulmonary Bypass, Principles and Practice.* 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008:417–418.

Murphy GS, Hessel EA, Groom RC, et al. Optimal perfusion during cardiopulmonary bypass: an evidence-based approach. *Anesth Analg.* 2009;108:1394–1417.

Yao FSF, Tseng CC, Woo D, et al. Maintaining cerebral oxygen saturation during cardiac surgery decreased neurological complications. *Anesthesiology.* 2001;95:A152.

C.II-28. How do you estimate the fluid balance during CPB?

During CPB, all intravenous lines are shut off. The intake includes cardioplegic solution, fluid or blood added to the oxygenator during CPB, and the decreased blood level in the oxygenator. The output includes urine and the increased blood level in the oxygenator.

C.II-29. How would you preserve the myocardium during CPB?

The most popular and effective method of protecting the myocardium is to reduce myocardial oxygen demand by hypothermia and cardioplegia. Hypothermia is induced by a combination of systemic blood cooling by heat exchangers in the oxygenator; local application of cold saline solution or iced slush to the external surface and chambers of the heart (if the heart is open); and infusion of cold cardioplegic solution through the aortic root, venous grafts, retrograde coronary sinus, or coronary ostium to the coronary arterial tree. The myocardial temperature may be decreased to 10° to 15° C (50° to 59° F).

In addition to inducing hypothermia and cardioplegia, one may take the following measures before aortic cross-clamping:

- Avoid tachycardia or increased contractility by discontinuing pacing at rapid rate and discontinuing inotropes if they were utilized.
- Initiate rapid arrest (asystole).
- Utilize proper venting methods and ensure adequate venous drainage to the pump to avoid ventricular distention, which decreases subendocardial blood supply.
- Prevent and treat ventricular fibrillation, which increases oxygen demand in normothermic myocardium.
- Maintain adequate coronary perfusion pressure of at least 50 mm Hg and greater than 70 mm Hg in the presence of severe coronary disease or left ventricular hypertrophy.

Gravlee GP, Davis RF, Kurusz M, et al. *Cardiopulmonary Bypass, Principles and Practice.* 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008:172–184.

C.II-30. What is the cardioplegic solution? How much would you use?

Cardioplegic solution contains mainly high concentrations of potassium (10 to 30 mEq per L) or magnesium (160 mEq per L) to relax the heart. Flaccid cardioplegia itself reduces myocardial oxygen consumption and provides optimal conditions for surgery. Bicarbonate or tris(hydroxymethyl)-aminomethane (THAM) is usually added to raise the pH to levels between 7.40 and 7.80 to increase the intracellular shift of potassium and to decrease the metabolic acidosis from ischemia. Steroids, calcium, and procaine may be added to stabilize lysosomal and cell membranes. Glucose and insulin are added to provide energy and improve the intracellular shift of potassium. Nitroglycerin is added to dilate coronary vessels, resulting in better perfusion to the myocardium, including ischemic areas. At the New York Presbyterian Hospital–Cornell Medical Center, for crystalloid cardioplegia, we add 20 mEq of potassium chloride and 10 mEq of sodium bicarbonate to 1,000 mL of 5% glucose in a 0.225% salt solution, resulting in a final pH of 7.83, potassium of 20 mEq per L, and osmolarity of 380 mOsm per L.

When blood cardioplegia is used, four parts of bypass blood are mixed with one part of cardioplegic solution. The composition of full-strength solution is as follows: 500 mL of 5% glucose in a 0.225% salt solution, 70 mEq of potassium chloride, 10 mEq of sodium bicarbonate, and 1 mg of nitroglycerin. Blood cardioplegia seems to have several advantages over crystalloid cardioplegia. The heart is arrested while being oxygenated, so that adenosine triphosphate (ATP) is not depleted before asystole. Repeated infusions provide a source of oxygen and glucose for continued metabolism and ATP repletion. Although little oxygen is released from hemoglobin during hypothermia, enough is probably dissolved in the plasma to sustain metabolism when reinfusion is performed every 30 minutes. Buffering capacity is improved because of the presence of the histidine buffering system present in red cells. Myocardial edema is reduced because of the osmolarity of blood. The risk of calcium paradox following ischemia is reduced and functional recovery is improved because of the physiologic calcium concentration provided by blood. The presence of red cell enzyme catalase may scavenge free radicals produced by ischemia. Capillary perfusion is improved and more homogeneous because of the presence of red cells. However, results of clinical studies in which blood cardioplegia was compared with crystalloid cardioplegia either detected no significant difference or showed that blood cardioplegia improved contractility late in the postoperative course. Multiple-dose cardioplegia is required for satisfactory results, whereas single-dose blood cardioplegia results in poor ventricular function.

Intermittent, continuous, or single infusions of cardioplegic solution have been used. Usually 300 to 600 mL of cold cardioplegic solution is needed to paralyze the myocardium and cool the myocardium to 10° to 20° C (50° to 68° F).

In the case of severe obstructive coronary lesions, antegrade infusion into the aortic root may cause maldistribution of the cardioplegia. Therefore, retrograde infusion through the coronary sinus into the coronary veins may be additionally employed to ensure homogeneous distribution of cardioplegia.

In the late 1980s and early 1990s, warm cardioplegia with near-systemic normothermia was popular for better myocardial protection. In a prospective randomized study by Franke et al., there was no difference in mortality, MI, IABP use, or postoperative inotropic requirements between patients receiving cold cardioplegia and those receiving warm cardioplegia. Patients receiving warm cardioplegia were less likely to require defibrillation following cross-clamp release, have less postoperative ventricular dysrhythmias, and a lower reoperation rate for bleeding. However, one study identified a threefold increase in strokes in the "warm" patients. The technique is no longer popular.

Franke UF, Korsch S, Wittwer T, et al. Intermittent antegrade warm myocardial protection compared to intermittent cold blood cardioplegia in elective coronary surgery—do we have to change? *J Cardiothorac Surg.* 2003;23:341–346.

Gravlee GP, Davis RF, Kurusz M, et al. *Cardiopulmonary Bypass, Principles and Practice.* 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008:172–184.

McLean RF, Wong BI. Normothermic versus hypothermic cardiopulmonary bypass: central nervous system outcomes. *J Cardiothorac Vasc Anesth.* 1996;10:45–53.

Shapiro N, Kirsh M, Jochim K, et al. Comparison of the effect of blood cardioplegia to crystalloid cardioplegia on myocardial contractility in man. *J Thorac Cardiovasc Surg.* 1980;80:647.

C.II-31. For how long a period can the aorta be cross-clamped?

When cardioprotective strategies including intermittent hypothermic blood cardioplegia, initiation of rapid arrest, and left ventricular venting are employed, the limits of "safe" ischemic time during aortic cross-clamping can be increased from as little as 15 to 45 minutes to as much as 240 minutes in animal models with normal ventricular function. However, many patients have preoperative ventricular dysfunction and the protection from hypothermic cardioplegia may not be optimal because of coronary artery obstruction. Clinically, the aorta may be safely cross-clamped for 60 to 120 minutes without perfusion. The shorter the cross-clamping time, the better the myocardial function will be.

Gravlee GP, Davis RF, Kurusz M, et al. *Cardiopulmonary Bypass, Principles and Practice.* 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008:217.

Rosenkranz GR, Buckberg CD. Myocardial protection during surgical coronary reperfusion. *J Am Coll Cardiol.* 1983;1:1235-1246.

C.II-32. Why would urine become pink in some cases of CPB? What is the renal threshold for plasma hemoglobin?

Pink urine is a sign of massive hemolysis. Hemolysis is mainly associated with the frothing, violent turbulence, acceleration, and shear forces of negative pressures generated by the suction apparatus and is associated to a lesser degree with the action of the pumps or with the gas–blood interface effects in the oxygenator. The renal threshold for hemoglobin is 100 to 150 mg per 100 mL. It is advisable to maintain a high output of alkaline urine to prevent possible tubular damage from acid hematin crystals, which are converted from hemoglobin.

Gravlee GP, Davis RF, Kurusz M, et al. *Cardiopulmonary Bypass, Principles and Practice*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008:42,59,99.

C.II-33. At what temperature can the patient be weaned from CPB?

An esophageal or nasopharyngeal temperature of 37° C (98.6° F) and a rectal or bladder temperature at least 35° C (95° F) must be reached before the patient can come off the pump. After discontinuation of the pump, surface warming should be continued in pediatric patients to prevent hypothermia owing to redistribution of heat in the body. However, in adults, the use of warming blankets and warmed humidified airway gases has not been found beneficial in preventing the expected temperature "afterdrop." Usually, esophageal or nasopharyngeal temperature will decrease and rectal or bladder temperature will increase during heat redistribution.

DiNardo JA, Schwartz MJ, eds. *Anesthesia for Cardiac Surgery*. Norwalk, CT: Appleton & Lange; 1990:236.

Gravlee GP, Davis RF, Kurusz M, et al. *Cardiopulmonary Bypass, Principles and Practice*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008:614–615.

C.II-34. Why does it take longer to rewarm than to cool the patient by the pump oxygenator?

It usually takes 5 to 10 minutes to cool the patient from 37° to 25° C (98.6° to 77° F) of average body temperature. It takes 20 to 40 minutes to rewarm the patient from 28° to 35° C (82.4° to 95° F). The speed of heat exchange by the bloodstream depends on the temperature gradient between venous blood and water in the heat exchanger, the pump blood-flow rate, and the water-flow rate of the heat exchanger. The initial venous blood temperature is 37° C (98.6° F) and the water temperature of the heat exchanger is 0° to 4° C (32° to 39.2° F) during cooling, creating a temperature gradient of 34° to 37° C (93.2° to 98.6° F). During rewarming, the water temperature is limited to 42° C (107.6° F) or less to prevent denaturation and destruction of blood proteins. The temperature gradient is limited to 10° C (18° F) or less to prevent gas embolism from a decrease of gas solubility in the blood associated with a sharp increase in temperature. The heat exchanger water flow does not differ much during cooling and rewarming. However, the pump blood flow is usually maintained to a very high level during the initial cooling because of low BP in the beginning of cooling. During rewarming, the pump blood flow is frequently maintained at a low level because the BP is usually high and the body temperature is still low. Rewarming may be accelerated by administering inhalation anesthetics, or employing vasodilators, to decrease vascular resistance and thereby increase pump flow to maintain the same BP. Because the increased vascular resistance is usually due to inadequate anesthesia during rewarming, we prefer inhalation anesthetics to vasodilators in patients with good ventricular function. In cases of poor ventricular function, inhalation agents are avoided because of the potential cardiac depression after CPB.

Gravlee GP, Davis RF, Kurusz M, et al. *Cardiopulmonary Bypass, Principles and Practice*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008:57–58.

Stanley TH, Berman L, Green O, et al. Plasma catecholamine and cortisol responses to fentanyl-oxygen anesthesia for coronary artery operations. *Anesthesiology*. 1980;53:250–253.

C.II-35. How would you defibrillate the heart internally during CPB?

The heart is defibrillated internally by a DC defibrillator, with 5 to 10 watt-seconds (joules). If the heart remains in ventricular fibrillation, blood gases, electrolytes, and temperature are rechecked and lidocaine, 1 to 2 mg per kg, is administered before repeated DC defibrillation attempts. MAP is usually increased to 80 mm Hg. Occasionally, esmolol, metoprolol, and amiodarone are added to treat intractable ventricular fibrillation or tachycardia.

Shanewise JS, Hines RL, Kaplan JA. Discontinuing cardiopulmonary bypass. In: Kaplan JA, Reich DL, Lake CL, et al., eds. *Kaplan's Cardiac Anesthesia.* 6th ed. Philadelphia: Elsevier Science, WB Saunders; 2011:992–1009.

C.II-36. Why is calcium chloride usually administered right before the patient comes off the pump?

With hemodilution, the ionized calcium frequently falls to approximately 1.5 to 1.8 mEq per L (normal 2.2 to 2.6 mEq per L, 1.1 to 1.3 mmol per L, or 4.5 to 5.6 mg per dL). Calcium chloride, 0.5 to 1.0 g, frequently is given to increase myocardial contractility and reverse potassium cardioplegia. Calcium increases the inotropic state of the myocardium and induces an increase in systemic vascular resistance that outlasts the inotropic effects. However, some believe that calcium administration is contraindicated at this time because of the compromised calcium hemostasis that accompanies the insult of aortic cross-clamping. Administration of calcium may exacerbate ischemic and reperfusion injury by causing accumulation of intracellular calcium. β-Blockers, on the other hand, increase intracellular calcium but also promote its reuptake into the sarcoplasmic reticulum and may be more appropriate in this setting. Therefore, use of calcium salts at the conclusion of bypass should be guided by determination of ionized calcium levels. Calcium salts should probably not be given to patients with good ventricular function in the absence of hypocalcemia or hyperkalemia because of the potential detrimental effects of iatrogenic hypercalcemia; whether this is true in patients with ventricular dysfunction is unknown.

Gravlee GP, Davis RF, Kurusz M, et al. *Cardiopulmonary Bypass, Principles and Practice*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008:299–301,615–616, 628.

Shanewise JS, Hines RL, Kaplan JA. Discontinuing cardiopulmonary bypass. In: Kaplan JA, Reich DL, Lake CL, et al., eds. *Kaplan's Cardiac Anesthesia.* 6th ed. Philadelphia: Elsevier Science, WB Saunders; 2011:992–1009.

C.II-37. If the HR is 40 beats per minute, what should you do?

A temporary atrioventricular (AV) block at the end of bypass because of potassium cardioplegia and ischemic insult during aortic cross-clamping. Although atropine may be theoretically administered to treat sinus or nodal bradycardia, more frequently, a temporary epicardial pacemaker is usually employed. Atrial pacing is preferred because of improved cardiac output when the atrial kick is preserved. Ventricular pacing is necessary if there is complete AV block. AV sequential pacing is indicated when ventricular pacing does not provide adequate cardiac output.

Shanewise JS, Hines RL, Kaplan JA. Discontinuing cardiopulmonary bypass. In: Kaplan JA, Reich DL, Lake CL, et al., eds. *Kaplan's Cardiac Anesthesia.* 6th ed. Philadelphia: Elsevier Science, WB Saunders; 2011:992–1009.

C.II-38. How does the blood sugar level change during CPB? Why? Does hyperglycemia increase neurologic complications during CPB?

Blood sugar levels are elevated during the perioperative period in patients undergoing cardiac surgery with the use of CPB. Hyperglycemia is most profound during hypothermic CPB, with approximately 100% of patients (diabetic and nondiabetic) achieving plasma glucose levels greater than 200 mg per dL. There are several reasons for this: First, the practice of making patients NPO (nothing by mouth) overnight induces a state of starvation, marked by peripheral resistance to insulin at the level of muscle and fatty tissues, therefore allowing glucose uptake by the brain; second, sympathoadrenal activation, in response to surgical stress, also tends to induce a diabetogenic state; third, active cooling the body during bypass causes a profound reduction in insulin production, induces peripheral insulin resistance, and is associated with renal tubular impairment in glucose regulation; lastly, use of dextrose-containing cardioplegia is a major contributor to intraoperative hyperglycemia. Of interest, postoperative hyperglycemia continues despite insulin administration and has been shown to remain above normal up to several weeks postoperatively. At the cellular level, the alterations in insulin receptor/resistance are very similar to that of type 2 diabetes. It is controversial whether hyperglycemia increases neurologic complications during CPB. Under conditions of limited cerebral oxygen delivery, anaerobic glucose oxidation becomes the primary method of ATP production, resulting in intracellular lactic acidosis. Hyperglycemia, by providing more glucose for anaerobic oxidation, increases the degree of intracellular acidosis, which, in numerous animal studies, correlates with the severity of subsequent injury. Although the deleterious effect of hyperglycemia in the face of both global and focal cerebral ischemia is generally accepted, a recent human study challenges these conclusions. Metz and Keats reported zero neurologic injury in a group of 54 patients undergoing CABG managed with glucose-containing fluids (glucose during bypass—approximately 700 ± 100 mg per dL) versus one stroke and one case of encephalopathy in 53 patients in whom glucose was avoided during CABG (glucose during bypass—approximately 200 ± 100 mg per dL). The authors contend that glucose does not affect neurologic outcome in the presence of a permanent focal lesion. Although provocative, this study can be faulted for (1) its lack of sensitive monitors of neurologic outcome, and (2) its small sample size in relation to the occurrence rate of the event of interest. More recently, there are a number of reports that show a strong association between plasma glucose levels and postoperative morbidity and mortality. In an observational study of 200 consecutive diabetic patients undergoing cardiac surgery, Ouattara demonstrated that poor intraoperative control of blood glucose concentrations was associated with an increased incidence of in-hospital morbidity, including neurologic, cardiovascular, infectious, respiratory, and renal. Based on these findings, "tight" glucose control is being recommended for all patients undergoing CPB. Murkin suggests avoidance of glucose containing intravenous, cardioplegic, and pump-priming solutions as well as aggressive insulin dosing strategies. Recent evidence suggests that this is best achieved with continous insulin infusion or hyperinsulinemic normoglycemic clamp technique. Regarding the optimal range of glucose control, there continues to be some debate about maintaining plasma glucose below the threshold of 110 mg per dL. Hypoglycemia remains a safety issue. Many authors suggest that a target glucose range of less than 150 mg per dL is favorable for maintaining euglycemia.

Carvalho G, Moore A, Schricker T, et al. Maintenance of normoglycemia during cardiac surgery. *Anesth Analg.* 2004;99:319–324.

Fontes ML, Koval KJ, Desvarieux T, et al. Epidemiology of hyperglycemia in nondiabetic patients undergoing hypothermic cardiopulmonary bypass. *Anesthesiology.* 2006;105:A749.

Fontes ML, Skubas N, Girardi L, et al. Glucosuria during cardiopulmonary bypass: does hypothermia provide protection or a blow to the kidneys? *Anesth Analg.* 2007;104:SCA81.

Gravlee GP, Davis RF, Kurusz M, et al. *Cardiopulmonary Bypass, Principles and Practice.* 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008:363–364, 388.

Grocott HP, Stafford-Smith M. Organ protection during cardiopulmonary bypass. In: Kaplan JA, Reich DL, Lake CL, et al., eds. *Kaplan's Cardiac Anesthesia.* 6th ed. Philadelphia: Elsevier Science, WB Saunders; 2006:992–993.

Lanier WL. Glucose management during cardiopulmonary bypass: cardiovascular and neurologic implications. *Anesth Analg.* 1991;72:423–427.

Metz S, Keats AS. Benefits of a glucose-containing priming solution for cardiopulmonary bypass. *Anesth Analg.* 1991;72:428–434.

Murkin JM. Pro: tight intraoperative glucose control improves outcome in cardiovascular surgery. *J Cardiothorac Vasc Anesth.* 2000;14:475–478.

O'Dwyer C, Prough DS, Johnston WE. Determinants of cerebral perfusion during cardiopulmonary bypass. *J Cardiothorac Vasc Anesth.* 1996;10:54–65.

Ouattara A, Lecomte P, Platonov I, et al. Poor intraoperative blood glucose control is associated with a worsened hospital outcome after cardiac surgery in diabetic patients. *Anesthesiology.* 2005;103:687–694.

Shann KG, Likosky DS, Murkin JM, et al. An evidence-based review of the practice of cardiopulmonary bypass in adults: a focus on neurologic injury, glycemic control, hemodilution, and the inflammatory response. *J Thorac and Cardiovasc Surg.* 2006;132:283–290.

Stanley TH, Berman L, Green O, et al. Plasma catecholamine and cortisol responses to fentanyl-oxygen anesthesia for coronary-artery operations. *Anesthesiology.* 1980;53:250–253.

Wass CT, Lanier WL. Glucose modulation of ischemic brain injury: review and clinical recommendations. *Mayo Clin Proc.* 1996;71:801–812.

C.II-39. What are the effects of CPB on platelet and coagulation factors?

Platelet dysfunction and thrombocytopenia are found on and after CPB. Platelet dysfunction is the most common cause of a bleeding problem following CPB after heparin is reversed and surgical bleeding is controlled. Transient defects in platelet plug formation and aggregation are seen in all patients put on CPB. Generally, platelet function returns to near normal status 2 to 4 hours following CPB. The defects are exacerbated and prolonged by drugs such as aspirin and platelet glycoprotein GPIIb/IIIa inhibitors (clopidogrel, tirofiban), which inhibit platelet function.

Platelet counts fall more with the bubble-type oxygenator than with the membrane-type oxygenator, but rarely below the levels clinically required for hemostasis. Thrombocytopenia is mainly caused by hemodilution, aggregation, adhesion, and the adenosine diphosphate–release reaction induced by the foreign surfaces and the blood–gas interface. Heparin may potentiate platelet aggregation and adhesions.

The level of coagulation factors decreases at the beginning of bypass because of hemodilution; surface absorption by the plastic, glass, and metal; and protein denaturation induced by the blood–gas interface. At the same time, the synthesis of clotting factors by the liver increases so that the concentration of clotting factors returns to normal within a period of hours. Membrane oxygenators cause few changes in clotting factors.

Gravlee GP, Davis RF, Kurusz M, et al. *Cardiopulmonary Bypass, Principles and Practice.* Philadelphia: Lippincott Williams & Wilkins; 2008:325–326, 427–428, 450–453.

C.II-40. How would you prepare for termination of CPB?

Before termination of CPB, cardiac and pulmonary function must be optimized. To ensure that all-important steps are not inadvertently omitted, the patient and all monitors should be carefully checked. The mnemonic LAMPS for Laboratory data, Anesthesia machine, Monitors, Patient (Pump), and Support is one useful approach.

Laboratory data

- Arterial pH, Pco_2, Po_2 within normal limits
- Hematocrit—20% to 25%
- K^+ —4.0 to 5.5 mEq per L
- Ionized calcium 1.1 to 1.2 mmol per L
- Pump mixed venous O_2 saturation greater than 70%

Anesthesia/Machine

- Adequate anesthesia
- Anesthesia machine functional

Monitors

- ECG—stable rate and rhythm (use pacing if necessary)
- Systemic BP restored to normothermic levels
- PA catheter functional
- Transducers rezeroed and calibrated
- TEE out of freeze mode
- Nasopharyngeal/PA catheter temperature 36° to 37° C (96.8° to 98.6° F)
- Bladder/rectal temperature greater than 35° C (95° F)

Patient/Pump

- The heart—contractility, size, rhythm, and air removed
- The lungs—atelectasis reexpanded, fluid in thoracic cavities drained, ventilation reinstituted

Support

- Inotropes/vasopressors/vasodilators
- IABP if needed

Gravlee GP, Davis RF, Kurusz M, et al. *Cardiopulmonary Bypass, Principles and Practice*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008:614–619.

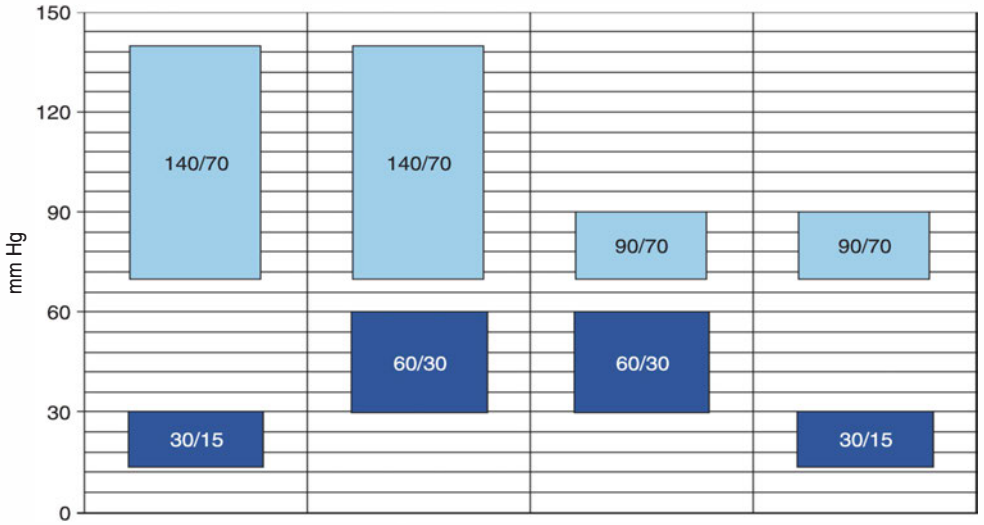
Shanewise JS, Hines RL, Kaplan JA. Discontinuing cardiopulmonary bypass. In: Kaplan JA, Reich DL, Lake CL, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: Elsevier Science, WB Saunders; 2011:992–1009.

Skubas NJ, Lichtman AD, Sharma A, et al. Anesthesia for cardiac surgery. In: Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1073–1107.

C.II-41. How would you decide the need for inotropic support?

The need for inotropic support after CPB is usually assessed by the following (Fig. 5.9):

- Preoperative ventricular function (ejection fraction)
- Effectiveness of intraoperative myocardial protection
- Adequacy of surgical repair
- Duration of aortic cross-clamping and CPB
- Patient's age



A		B		C		D	
CO↑	CO↓	CO↑	CO↓	CO↑	CO↓	CO↑	CO↓
Hyperdynamic	↑↑SVR ?↓Volume	Too full	↑Vascular tone ?contractility	↑SVR Too full	↓↓Contractility ALARM	↓↓SVR	↓Volume ↓Contractility ↑CVP: RV failure?
Wait ↑Depth	Dilate ± Volume	Wait Dilate	Dilate ± Inotrope	Wait ↑Vascular tone	Adjust preload Inotrope (?IABP, LVAD) ↑tone	↑Tone	↑preload Inotrope NO, PGL_2 (unload RV) (?IABP, LVAD) ↑Perfusion pressure

Figure 5.9 Hemodynamic management during weaning from cardiopulmonary bypass. The hemodynamic evaluation is performed by combining information from the systemic (light shade boxes) and pulmonary (black boxes) arterial pressures. **A.** A combination of elevated systemic arterial and low pulmonary arterial pressure suggests either a hyperdynamic cardiac function (if cardiac output is high) or a vasoconstrictive state (if the peripheral vascular resistance is high). **B.** If systemic hypertension is accompanied by pulmonary hypertension, then either the volume status is elevated (if cardiac output is high), or there is generalized vasoconstriction (if cardiac output is decreased). **C.** In case of systemic hypotension and pulmonary hypertension, the cardiac output may be high (systemic vasodilation) or low (depressed contractility, requiring immediate intervention). **D.** When both systemic and pulmonary pressures are decreased, there is either vasodilation (if the cardiac output is high) or hypovolemia or depressed contractility or right-sided failure are suspected (if cardiac output is decreased). The relative treatment for each hemodynamic derangement is shown in the table. CO, cardiac output; CVP, central venous pressure; IABP, intra-aortic balloon pump; LVAD, left ventricular assist device; NO, nitric oxide; PGI_2, prostacyclin; RV, right ventricle; SVR, systemic vascular resistance; ↑, increase; ↑↑, marked increase; ?, questionable.

If LV ejection fraction is predicted to be 25% to 35%, milrinone infusion may be added. Norepinephrine infusion is usually needed during milrinone therapy. Generally, IABP is also employed when LV ejection fraction is predicted to be below 25%. The choice of vasoactive and cardioactive agents used is frequently center and/or physician specific and, in most cases, initiated as prophylaxis. Recent data suggest that this practice should be avoided because inotropic and vasopressors can have negative effects, which can result in both morbid and fatal events.

Gravlee GP, Davis RF, Kurusz M, et al. *Cardiopulmonary Bypass, Principles and Practice*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008:619–629.

Shanewise JS, Hines RL, Kaplan JA. Discontinuing cardiopulmonary bypass. In: Kaplan JA, Reich DL, Lake CL, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: Elsevier Science, WB Saunders; 2011:992–1009.

C.III. *After Cardiopulmonary Bypass*

C.III-1. How would you reverse heparin? How much protamine would you use? What are the other drugs used to neutralize heparin?

It has been recommended that 1.1 to 1.3 mg of protamine sulfate is needed to reverse each 100 units of remaining heparin calculated by ACT dose-response curve or protamine titration test. At the New York Presbyterian Hospital–Cornell Medical Center, we give 1.0 mg of protamine to reverse each 100 units or 1 mg of heparin initially administered. Only the initial dose of heparin is counted. The subsequently added dose of heparin, to keep the ACT level above 480 seconds, is not considered because of its metabolism and elimination. The ACT test is repeated 10 minutes after the administration of protamine. ACT usually returns to its control level. If the ACT is still prolonged, additional protamine is given according to the ACT dose-response curve. However, the ACT is affected by dilution and by hypothermia; dose-response curves utilizing data obtained during hypothermia may be misleading. In addition, severe thrombocytopenia also prolongs the ACT because clot formation using the ACT depends on platelet phospholipid surface. Furthermore, because heparin rebound is possible, it may be optimal to administer protamine at two times following CPB: once after bypass and again 1 or 2 hours later to counteract heparin rebound. Of note, recent work by Bollinger and colleagues suggests that increase in bleeding may occur paradoxically from "extra" protamine administration.

Other drugs that have been used to neutralize heparin include platelet factor 4 (PF4), heparinase, protamine variants, polybrene, and toluidine blue. Human or recombinant PF4 has been used in animals and humans to reverse heparin and does not cause systemic arterial hypotension, or pulmonary hypertension, or changes in white blood cell count, platelet count, or complement levels. Heparinase neutralizes heparin by enzymatic cleavage of α-glycoside linkages at AT III binding site. Heparinase is an effective antagonist of heparin and has minimal effects on platelets, whereas protamine markedly inhibits platelet responsiveness. It appears to be a potential alternative to protamine.

Two protamine variants, so-called designer protamines, are currently under investigation. The side effects of protamine such as hypotension and low cardiac output were significantly reduced by the protamine variants. Polybrene, also known as hexadimethrine bromide, at one time was commonly used, but it was withdrawn from clinical use because of suspected nephrotoxicity and production of pulmonary hypertension. Toluidine blue has also been used for heparin reversal, but it is less effective than protamine and is associated with methemoglobinemia.

Lastly, reversal for low molecular weight heparin compounds does not exist, but recently a recombinant antithrombin variant was shown to be a potent antidote to fondaparinux and other heparin derivatives.

Bianchini EP, Fazavana J, Picard V, et al. Development of a recombinant antithrombin variant as a potent antidote to fondaparinux and other heparin derivatives. *Blood*. 2011;117:2054–2060.

Bolliger D, Szlam F, Azran M, et al. The anticoagulant effect of protamine sulfate is attenuated in the presence of platelets or elevated factor VIII concentrations. *Anesth Analg*. 2010;111(3):601–608.

Gravlee GP, Davis RF, Kurusz M, et al. *Cardiopulmonary Bypass, Principles and Practice*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008:473–478.

Nielsen VG, Malayaman SN. Protamine sulfate: crouching clot or hidden hemorrhage? *Anesth Analg*. 2010;111(3):593–594.

Spiess BD, Horrow J, Kaplan JA. Transfusion medicine and coagulation disorders. In: Kaplan JA, Reich DL, Lake CL, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: Elsevier Science, WB Saunders; 2006:958–966.

C.III-2. What is the action mechanism of protamine?

Heparin is a strong organic acid (polyanion). Protamine is a strong organic base (polycation). They combine ionically to form a stable salt and lose their own anticoagulant activity. Protamine contains two active sites, one that neutralizes heparin and another that exerts a mild anticoagulant effect independent of heparin.

Gravlee GP, Davis RF, Kurusz M, et al. *Cardiopulmonary Bypass, Principles and Practice*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008:471.

Spiess BD, Horrow J, Kaplan JA. Transfusion medicine and coagulation disorders. In: Kaplan JA, Reich DL, Lake CL, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: Elsevier Science, WB Saunders; 2006:959.

C.III-3. What are the complications of too much protamine?

Protamine itself is an anticoagulant. Protamine administered intravenously in the absence of heparin interacts with platelets and with many clotting proteins. Protamine induces transient thrombocytopenia in humans. Platelet aggregation is impaired by the protamine–heparin complex, but protamine alone has no deleterious effects. Protamine may bind to thrombin and inhibit thrombin's ability to convert fibrinogen to fibrin.

Bolliger D, Szlam F, Azran M, et al. The anticoagulant effect of protamine sulfate is attenuated in the presence of platelets or elevated factor VIII concentrations. *Anesth Analg*. 2010;111(3):601–608.

Gravlee GP, Davis RF, Kurusz M, et al. *Cardiopulmonary Bypass, Principles and Practice*. Philadelphia: Lippincott Williams & Wilkins; 2000:473.

Nielsen VG, Malayaman SN. Protamine sulfate: crouching clot or hidden hemorrhage? *Anesth Analg*. 2010;111(3):593–594.

Spiess BD, Horrow J, Kaplan JA. Transfusion medicine and coagulation disorders. In: Kaplan JA, Reich DL, Lake CL, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: Elsevier Science, WB Saunders; 2011:949–991.

C.III-4. Why did the patient develop hypotension after protamine was administered? How do you treat and prevent this condition?

Three different types of circulatory reactions to protamine reversal of heparin have been proposed by Horrow:

Type I: Systemic Hypotension from Rapid Injection: A Predictable Pharmacologic Reaction

Type II: Anaphylactic or Anaphylactoid Reaction

- Antibody-medicated
- Immediate anaphylactoid response without antibody involvement
- Delayed anaphylactoid response (noncardiac pulmonary edema)

Type III: Catastrophic Pulmonary Vasoconstriction with Systemic Hypotension

However, etiologically, there are only two types of reaction: (1) pharmacologic side-effect reactions, and (2) idiosyncratic reactions. Therefore, an alternative classification was proposed by Moorman, Zapl, and Lowenstein as follows:

- Pharmacologic histamine release
- True anaphylaxis (immunoglobulin E–mediated)
- Anaphylactoid reactions
- Pulmonary vasoconstriction
- Noncardiogenic pulmonary edema

Mild to moderate systemic hypotension from pharmacologic side effects is almost always the reaction seen when protamine is given rapidly or is given to patients who are relatively hypovolemic and vasoconstricted. Because it can be elicited in most patients, it is classified as a pharmacologic side effect, not an idiosyncratic reaction. This side effect is possibly mediated by histamine and is characterized by venodilation, reduced cardiac filling pressures, and decreased vascular resistance. Mild cardiac depression by protamine is suggested but probably does not occur. This type of hypotension can be corrected by rapid volume administration from the CPB pump while the arterial cannula is in place and by administration of phenylephrine in 0.1-mg increments. There have been many attempts to modify the hypotensive response (e.g., intra-aortic or left atrial administration, protamine pretreatment), with little evidence of predictable success. Only slower rates of intravenous infusion over 5 to 10 minutes and simultaneous maintenance of an adequate blood volume have been shown to decrease the incidence of hypotension.

Anaphylactic or anaphylactoid reaction is uncommon and rarely seen in infants and children. The reaction varies from mild skin flushing and urticaria to severe vascular collapse. Systemic hypotension is usually accompanied by low pulmonary arterial pressure and low right-sided and left-sided filling pressures. This type of hypotension may be treated and prevented with rapid volume infusion and administration of vasoconstrictors. The use of antihistamines and steroids is commonly employed by many cardiovascular anesthesiologists with few, if any, existing data supporting this practice. There are several unanswered questions such as: When should these angents be given? What dose to give? Which agent? and so forth. Diabetic patients taking neutral protamine Hagedorn (NPH) insulin may develop antibodies to protamine and would appear to be at increased risk. However, clinical reactions do not predictably occur in these patients. Suspected cross-sensitivity in cases of fish allergy or autosensitization in men after vasectomy do not seem to put most patients at increased risk.

Catastrophic pulmonary hypertension occurs in approximately 0.2% to 4.0% of patients. There are severalfold increases in PA pressure leading to right ventricular failure, elevated CVP, low flow across the pulmonary circuit, and low left atrial pressure. Elevated plasma levels of C5a anaphylatoxins and thromboxane are responsible for pulmonary vasoconstriction and accompanied bronchoconstriction. Treatment with isoproterenol, milrinone, or amrinone is reasonable; epinephrine in 0.1-mg increments has been successfully used. If severe hypotension persists, the patient should be heparinized again and return to bypass to maintain circulation. A recent study has shown that left ventricular infusion of protamine provides no protection from pulmonary hypertension and that histamine and platelet-activating factors are not involved in acute pulmonary vasoconstriction. Therefore, antihistamines and steroids may not be effective in preventing this reaction. However, it has been shown that the rate of intravenous protamine infusion in sheep is an important factor in the generation of sufficient mediators required to initiate a characteristic physiologic response, including pulmonary vasoconstriction and thromboxane B_2 generation. Slowing the

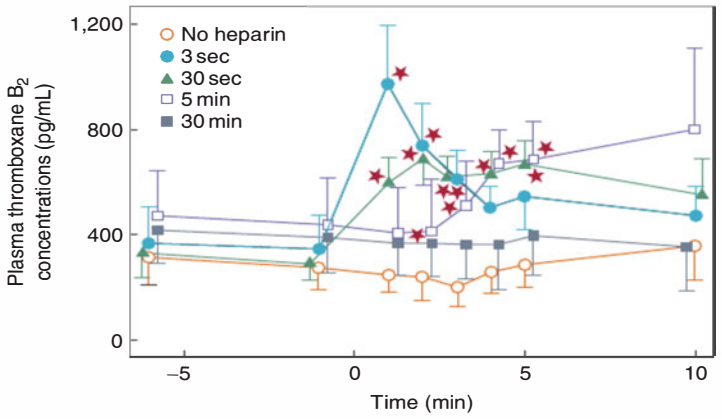


Figure 5.10 Plasma thromboxane B_2 concentrations before and after administration of protamine infused over 3 seconds, 30 seconds, 300 seconds, and 30 minutes. Heparin is injected at 5 minutes; protamine infusion is started at 0 minutes. Data points represent mean ± SE values; n = 6 in each group ($P < .05$ from unheparinized group). (From Morel DR, Costabella PM, Pittet JF. Adverse cardiopulmonary effects and increased plasma thromboxane concentrations following the neutralization of heparin with protamine in awake sheep are infusion rate-dependent. *Anesthesiology*. 1990;73:415–424, with permission.)

rate of protamine infusion results in a proportional attenuation of the response (Figs. 5.10 and 5.11).

In conclusion, the treatment of hypotension after protamine administration depends on pulmonary arterial pressure. Hypotension with low pulmonary arterial pressure may be corrected with rapid volume infusion and vasoconstrictors, and hypotension with high pulmonary arterial pressure should be treated with inotropes that have a vasodilating effect. The only effective prevention is a slow infusion of diluted protamine solution.

Recently, Yang developed a reactor device containing immobilized protamine (defined as a protamine bioreactor) that can be placed on the distal end of the extracorporeal CPB circuit. The protamine bioreactor binds and selectively removes heparin in the extracorporeal device before it is returned to the patient. The device successfully prevents protamine-induced complications in dogs. It is hoped that in the near future, the device can be used clinically to remove heparin without administration of protamine to the patients.

Coleman RN. Humoral mediators of catastrophic reactions associated with protamine neutralization. *Anesthesiology*. 1987;66:595–596.

Gravlee GP, Davis RF, Kurusz M, et al. *Cardiopulmonary Bypass, Principles and Practice*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008:480–488.

Habazettl H, Conzen PF, Vollmar B, et al. Pulmonary hypertension after heparin-protamine: roles of left-sided infusion, histamine and platelet activation factor. *Anesth Analg*. 1990;71:637–637.

Kien ND, Quam DD, Reitan JA, et al. Mechanism of hypotension following rapid infusion of protamine sulfate in anesthetized dogs. *J Cardiothorac Vasc Anesth*. 1992;6:143–147.

Morel DR, Costabella PM, Pittet JF. Adverse cardiopulmonary effects and increased plasma thromboxane concentrations following the neutralization of heparin with protamine in awake sheep are infusion rate-dependent. *Anesthesiology*. 1990;73:415–424.

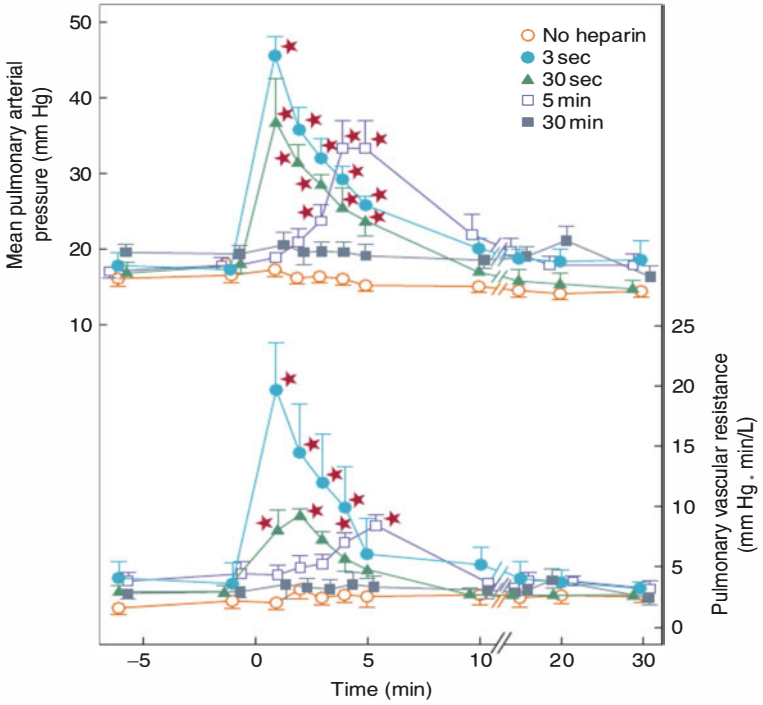


Figure 5.11 Pulmonary hemodynamics before and after administration of protamine infused over 3 seconds, 30 seconds, 300 seconds, and 30 minutes. Heparin is injected at 5 minutes; protamine infusion is started at 0 minutes. Data points represent mean ± SE values; n = 6 in each group ($P < .05$ from unheparinized group). (From Morel DR, Costabella PM, Pittet JF. Adverse cardiopulmonary effects and increased plasma thromboxane concentrations following the neutralization of heparin with protamine in awake sheep are infusion rate-dependent. *Anesthesiology.* 1990;73:415–424, with permission.)

Spiess BD, Horrow J, Kaplan JA. Transfusion medicine and coagulation disorders. In: Kaplan JA, Reich DL, Lake CL, et al., eds. *Kaplan's Cardiac Anesthesia.* 6th ed. Philadelphia: Elsevier Science, WB Saunders; 2011:949–991.

C.III-5. What are the indications for intra-aortic balloon pump (IABP)?

IABP is primarily used for pump failure and myocardial ischemia that are not responsive to maximal pharmacologic support. The indications include the following:

Ischemic heart disease

- Cardiogenic shock
- Acute MI complicated by
  - Mechanical defects: ventricular or septal rupture, acute mitral insufficiency, or ventricular aneurysm
  - Continued ischemic pain and extension of infarction
  - Refractory ventricular arrhythmias
- During cardiac catheterization

- Undergoing noncardiac surgery
- Failed PCI and awaiting CABG
- Acute mitral insufficiency with CHF

Cardiac surgery

- Before CPB and postoperatively
- After CPB: low output syndrome

Pulsatile CPB. Rare
Pediatric congenital heart disease. Rare
Neurosurgery. Temporarily increases total cerebral blood flow in specific circumstances.

Gravlee GP, Davis RF, Kurusz M, et al. *Cardiopulmonary Bypass, Principles and Practice*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008:135–136.

Shanewise JS, Hines RL, Kaplan JA. Discontinuing cardiopulmonary bypass. In: Kaplan JA, Reich DL, Lake CL, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: Elsevier Science, WB Saunders; 2011:992–1009.

Skubas N, Lichtman AD, Sharma A, et al. Anesthesia for cardiac surgery. In: Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1073.

C.III-6. What are the principles of IABP?

IABP counterpulsation is designed to increase the myocardial oxygen supply during diastole and to decrease myocardial oxygen demand during systole (Fig. 5.12). The balloon is inflated during diastole to increase the diastolic aortic pressure, resulting in increased coronary blood flow. The balloon should be inflated immediately following the closure of the aortic valve at the dicrotic notch of arterial tracing. The balloon is deflated just before the next systole to decrease the intra-aortic pressure and afterload, resulting in decreased myocardial oxygen consumption. The cardiac output is increased because of increased coronary perfusion (diastolic augmentation) and decreased resistance (systolic unloading).

Gravlee GP, Davis RF, Kurusz M, et al. *Cardiopulmonary Bypass, Principles and Practice*. Philadelphia: Lippincott Williams & Wilkins; 2008:135–136.

Shanewise JS, Hines RL, Kaplan JA. Discontinuing cardiopulmonary bypass. In: Kaplan JA, Reich DL, Lake CL, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: Elsevier Science, WB Saunders; 2011:992–1009.

Skubas N, Lichtman AD, Shaarma A, et al. Anesthesia for cardiac surgery. In: Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia: Lippincott Williams & Wilkins 2009:1073.

C.III-7. What are the complications of IABP?

- Ischemia of the leg
- Dissection of the aorta
- Thrombus formation and embolization
- Renal artery occlusion
- Splenic, mesenteric, and spinal cord infarction
- Internal mammary occlusion
- Thrombocytopenia
- Infection
- Gas embolization

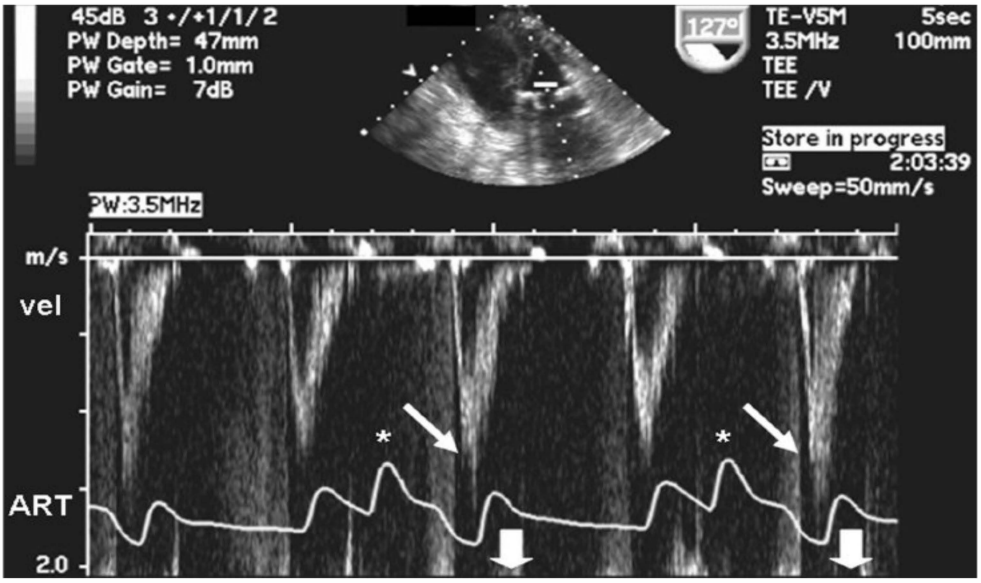


Figure 5.12 The function of the intra-aortic balloon pump (IABP). In this patient with an IABP in place, the velocity (vel) of the blood flow, as it exits the left ventricle (LV), is recorded. The arterial waveform is shown in the following text. The IABP is set on a 1:2 ratio; that is, it inflates every other beat, in diastole (*asterisks*). The velocity (and the amount) of blood exiting the LV is increased (*arrows*) after the diastolic inflation of the IABP because the LV is ejecting against lower systemic resistance. This is the reason that the systolic arterial pressure following IABP inflation is lower (*down arrows*).

- Inability to place the IABP
- Retroperitoneal bleeding
- Arterial–venous fistula

Gravlee GP, Davis RF, Kurusz M, et al. *Cardiopulmonary Bypass, Principles and Practice*. Philadelphia: Lippincott Williams & Wilkins; 2008:435–442.

Shanewise JS, Hines RL, Kaplan JA. Discontinuing cardiopulmonary bypass. In: Kaplan JA, Reich DL, Lake CL, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: Elsevier Science, WB Saunders; 2011.

Skubas N, Lichtman AD, Sharma A, et al. Anesthesia for cardiac surgery. In: Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1073.

C.III-8. Can PAOP represent left ventricular end-diastolic volume (LVEDV) after CABG?

It has been demonstrated that in nonsurgical patients, there was a significant correlation between changes in PAOP and LVEDV. However, in patients during the first few hours after CABG, there was a poor correlation between changes in PAOP and LVEDV. The poor correlation was not explained by changes in systemic or pulmonary vascular resistance. The altered ventricular pressure–volume relation may reflect acute changes in ventricular compliance. Although measurement

of PAOP remains valuable in clinical management to avoid pulmonary edema, it cannot reliably be used as an index of left ventricular preload while attempting to optimize stroke volume. TEE can accurately assess LVEDV and cardiac contractility.

Harsen RM, Viquerat CE, Matthay MA, et al. Poor correlation between pulmonary arterial wedge pressure and left ventricular end-diastolic volume after coronary artery bypass graft surgery. *Anesthesiology*. 1986;64:764–770.

Reich DL, Mittnacht A, London M, et al. Monitoring of the heart and vascular system. In: Kaplan JA, Reich DL, Savino JS, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: Elsevier Saunders; 2011:416–451.

D. Postoperative Management

D.1. What are the postoperative complications?

Cardiovascular. CHF, arrhythmias, low output syndrome, myocardial ischemia or infarction due to surgical manipulation, prolonged CPB and aortic cross-clamp (coronary ischemia), use of cardioplegic solution, and occlusion or kinking of grafts.

Pulmonary. Acute lung injury or adult respiratory distress syndrome due to the following:

- Decreased blood flow to the lung during total CPB
- Collapsed alveoli during CPB, resulting in decreased surfactant and decreased distensibility
- Fluid overloading
- Hyperoxia during CPB
- Left ventricular failure
- Microemboli
- Reperfusion injury
- Inflammatory response
- Infections
- Transfusion-related lung dysfunction

Renal

- Polyuria from hemodilution and diuretics
- Oliguria from hypoperfusion
- Acute kidney injury
  - Hypoperfusion
  - Ischemia
  - Inflammatory response
  - Neprotoxins (preoperative contrast dyes, antibiotics)
- Acute tubular necrosis
- Acute or chronic renal insufficiency

Hemorrhage

- Too much or too little protamine to reverse heparin
- Thrombocytopenia and decreased coagulation factors
- Qualitative and quantitative platelet defect
- Disseminated intravascular coagulopathy
- Fibrinolysis with low levels of fibrinogen
- Poor surgical hemostasis

Embolism. Due to air, destroyed or aggregated formed blood elements, fat, endogenous and exogenous debris.
Neurologic. Stroke and neurocognitive dysfunction marked by functional changes in behavior, personality, or other brain functions; cerebral embolism; and seizures.
Hyperglycemia. Hypothermia, dextrose-containing cardioplegia, increased catecholamine levels, and diabetogenic state associated with sugery and CPB.
Hypopotassemia. Due to hemodilution, alkalosis, and diuretics.

Gravlee GP, Davis RF, Kurusz M, et al. *Cardiopulmonary Bypass, Principles and Practice*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008:382, 403, 506, 628–629.

Levy JH, Tanaka K, Bailey JM, et al. Postoperative cardiovascular management. In: Kaplan JA, Reich DL, Lake CL, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: Elsevier Science, WB Saunders; 2011:98-131.

D.2. Would you reverse the muscle relaxants? Why?

Yes and no. If early extubation (fast-track) is planned, short- or intermediate-acting muscle relaxants should be used after CPB and the neuromuscular function should be monitored. At the end of the procedure, reversal agent can be given to ensure that the patient does not experience paralysis while awake. It may be advisable to continue a short-acting sedative/hypnotic agent such as propofol or midazolam during transport to the ICU and for the immediate period required to establish criteria for extubation. In patients that are hemodynamically unstable, with profound hypoxemia (acute respiratory distress syndrome), and/or "open" chest, paralysis should be continued postoperatively until the clinical state has improved. However, it is important to recognize that prolonged paralysis can lead to marked skeletal myopathy.

D.3. When will you wean the patient from the respirator?

Ventilator mangement, weaning strategy, and extubation time vary significantly among centers practicing cardiac surgery. Historically, patients were weaned from the respirator the following morning after surgery. More recently, if the operative course is smooth and if the patient is hemodynamically stable, weaning and extubation can be performed early (usually 2 to 6 hours after surgery).

Early tracheal extubation (fast-track) after CABG surgery may have cost-benefits and improvement in resource use when compared with late tracheal extubation. In one report, early tracheal extubation 1 to 6 hours after surgery reduced total cost per CABG surgery by 25% without increasing the rate or costs of complications in patients younger than 75 years.

Cheng DC, Havski J, Peniston C, et al. Early tracheal extubation after coronary artery graft surgery reduces costs and improves resource use. *Anesthesiology*. 1996;85:1300–1310.

Higgins TL, Yared J-P. Postoperative respiratory care. In: Kaplan JA, Reich DL, Lake CL, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: Elsevier Science, WB Saunders; 2011:1046–1060.

D.4. What criteria would you use in deciding when to wean the patient from the respirator?

- Consciousness—awake and alert
- Stable vital signs
- Acceptable arterial blood gases—pH, 7.35 to 7.45; Pao_2, over 80 mm Hg with FIo_2,0.4; $Paco_2$, 35 to 45 mm Hg

- Acceptable respiratory mechanics
- Vital capacity greater than 10 to 15 mL per kg
- Maximal inspiratory force—greater than 20 to 25 cm H_2O
- Hemostasis—less than 100 mL per hour of chest tube drainage
- Stable metabolic state—normal temperature and electrolytes

The patient should tolerate being on continuous positive airway pressure of 5 cm H_2O and pressure support of 5 cm H_2O with 40% oxygen. If the patient tolerates the continuous positive airway pressure well for 30 minutes and arterial blood gases are acceptable, the patient may be extubated.

Higgins TL, Yared J-P. Postoperative respiratory care. In: Kaplan JA, Reich DL, Lake CL, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: Elsevier Science, WB Saunders; 2011:1046–1060.

CHAPTER 6

Valvular Heart Disease

Natalia S. Ivascu and Gregg S. Hartman

A 78–YEAR-OLD MAN

was admitted with increasing shortness of breath. He had chest pain in the past but was able to continue with normal activities. He had passed out twice in the past year. On physical examination, a loud systolic murmur could be heard at the left sternal border radiating to the neck. His vital signs were: blood pressure 150/90 mm Hg, heart rate 88 beats per minute and irregular. The electrocardiogram showed sinus rhythm with atrial premature contractions and left ventricular hypertrophy (LVH) with strain. A transthoracic echocardiogram (TTE) showed a hypertrophied left ventricle, and Doppler examination demonstrated severe aortic stenosis with a gradient of 64 mm Hg, mild aortic insufficiency, and moderate mitral regurgitation. He was scheduled for aortic valve replacement and possible mitral valve repair or replacement.

A. Medical Disease and Differential Diagnosis

1. What are the major etiologies of aortic stenosis, aortic insufficiency, mitral stenosis, and mitral regurgitation?
2. What are the major changes in the loading conditions of the left ventricle that result from the four different lesions? Why do they occur? What changes result from them?
3. What are pressure–volume (P–V) loops? What do the different inflection points represent?
4. What are representative P–V loops for the four valvular lesions?
5. Draw the pressure/time curves for the left ventricle, left atrium, pulmonary artery, and aorta for a normal patient and for patients with each of the four valvular lesions.
6. What are the basic principles of echocardiography? What are M-mode, B-mode, and Doppler color modalities? How do TTE and transesophageal echocardiography (TEE) differ?
7. What are the three TEE vantage points for the comprehensive imaging of the left ventricle? How are pressure gradients measured by echocardiography?

How do the pressure gradients derived from Doppler echocardiography differ from those obtained in the catheterization laboratory by direct pressure measurement?

8. What is the role for three-dimensional (3D) echocardiography in the operating room?
9. What are the echocardiographic and cardiac catheterization criteria for the four valvular lesions?

B. Preoperative Evaluation and Preparation

1. What are the presenting signs and symptoms of the four valvular lesions listed previously?
2. What is the New York Heart Association classification of heart failure?
3. Discuss the role of premedication for patients with the four different valvular lesions.
4. How would you premedicate the patient with severe atrial stenosis and mitral regurgitation?

C. Intraoperative Management

1. Outline the hemodynamic management goals for each of the four valvular lesions. What are the anesthetic goals with respect to heart rate and rhythm, preload, afterload, and contractility?
2. What are the hemodynamic goals for this patient with the combination of severe aortic stenosis and mitral regurgitation?
3. How would you monitor this patient with severe atrial stenosis and mitral regurgitation?
4. Should the patient have a pulmonary artery catheter placed before induction?
5. Is a pulmonary artery catheter with pacing capabilities indicated?
6. What anesthetic technique would you employ? Why?
7. What muscle relaxant would you use for this patient?
8. What are the usual TEE findings in a patient with aortic stenosis, aortic insufficiency, or mitral regurgitation? How do you grade the severity of aortic stenosis by TEE? How do you quantify the severity of mitral regurgitation? What is the impact of aortic stenosis on the severity of mitral regurgitation?
9. What special considerations particular to cardiopulmonary bypass (CPB) operations do you have for each of the four lesions? Focus on these concerns with respect to the induction and prebypass, bypass, and postbypass periods.
10. The patient cannot be weaned from CPB following an aortic valve replacement and mitral valve replacement. What are the possible causes?
11. How would you diagnose right heart failure and pulmonary hypertension? How would you treat it?
12. How does an intra-aortic balloon pump (IABP) work to benefit the failing heart?
13. What role does the IABP have in this setting?
14. What role does TEE play in the placement, timing, and demonstration of efficacy of an IABP?
15. How would you properly time the IABP cycle?
16. What are the contraindications to the use of an IABP?
17. What is the role for ventricular assist devices?

D. Postoperative Management

1. In the intensive care unit (ICU) 4 hours later, the patient became hypotensive with a low cardiac output. How could you distinguish between cardiac tamponade and pump failure? How would the TEE images differ?

2. Would you extubate this patient early in the ICU? Why?
3. What are the advantages and disadvantages of early extubation?

E. Alternative treatments

1. What are the percutaneous options for mitral valve repair?
2. How is percutaneous mitral valve repair performed?
3. What are the percutaneous options for aortic valve repair and replacement?
4. How is percutaneous aortic valve replacement performed?
5. What anesthetic techniques and monitors are used?
6. What is minimally invasive cardiac valve surgery?

A. Medical Disease and Differential Diagnosis

A.1. What are the major etiologies of aortic stenosis, aortic insufficiency, mitral stenosis, and mitral regurgitation?

Aortic stenosis occurs as a congenital lesion but more commonly as an acquired disease. Stenosis may develop on a previously normal valve following rheumatic fever or from progressive calcification. Congenitally bicuspid valves are also prone to calcification with eventual stenosis. Calcification of the leaflets can result in incomplete closure of the valve with associated insufficiency.

Aortic insufficiency is usually an acquired disease. The most common causes include bacterial endocarditis and rheumatic heart disease. Annular dilation may result from diseases such as cystic medial necrosis and collagen disorders or following aortic dissections with resultant insufficiency. When occurring as a congenital lesion, aortic insufficiency rarely occurs in the absence of other cardiac abnormalities.

Mitral stenosis is almost always caused by rheumatic fever, although only half of patients will have a history of an acute febrile illness. The inflammatory process of rheumatic fever results in thickening of the leaflets and fusion of the commissures. Other rare causes include congenital stenosis and other systemic diseases, including systemic lupus erythematosus and carcinoid. Pathophysiology similar to that seen with valvular mitral stenosis can occur with obstructing left atrial tumors and cor triatriatum. Mitral stenosis commonly occurs in conjunction with other valvular heart disease; only 25% of patients present with isolated mitral stenosis, and approximately 40% have combined mitral stenosis and mitral regurgitation.

Mitral regurgitation can result from defects in the leaflets, the annular ring or the supporting chordae, the papillary muscles, or any combination of these. Primary leaflet dysfunction occurs with rheumatic fever but can also follow bacterial endocarditis, connective tissue disorders, and congenital malformations. Annular dilation can follow ventricular dysfunction and left ventricular dilation. Mitral valve prolapse and rupture of papillary muscles result in incomplete leaflet closure or coaptation with resultant mitral regurgitation. Left ventricular ischemia can affect papillary muscle contraction and is the cause of postischemic or postinfarction mitral regurgitation.

Hartman GS. *Management of Patients with Valvular Heart Disease*. Cleveland: International Anesthesia Research Society; 1994:141–151. 1994 IARS Review Course Lectures.

Schoen FJ. Cardiac valves and valvular pathology: update on function, disease, repair, and replacement. *Cardiovasc Pathol*. 2005;14:189–194.

Thys DM, Hillel Z, Schwartz AJ, eds. *Textbook of Cardiothoracic Anesthesiology*. New York: Graw-Hill; 2001:589–629.

A.2. What are the major changes in the loading conditions of the left ventricle that result from the four different lesions? Why do they occur? What changes result from them?

Aortic stenosis represents a chronic systolic pressure load on the left ventricle. This elevation increases wall tension in accordance with Laplace's law.

$$\text{Wall tension} = \frac{(\text{Pressure} \times \text{Radius})}{(2 \times \text{Wall thickness})}$$

The ventricle undergoes parallel duplication of muscle fibers in an attempt to compensate for the increase in tension. This results in increased wall thickness or concentric (common center) hypertrophy and some decrease in radius, thereby normalizing wall stress. If the mitral valve remains competent, the major pressure overload occurs in the left ventricle and little change in the other cardiac chambers results.

Aortic insufficiency causes left ventricular diastolic volume overload, resulting in eccentric (away from the center) hypertrophy and left ventricular dilation. Compliance, the relation between volume and pressure, is altered only slightly because both end-systolic and end-diastolic volumes increase. Some concentric hypertrophy occurs as well secondary to the increase in wall stress resulting from an increase in left ventricular radius. The aortic diastolic pressure is lower with aortic insufficiency. Remember, the diastolic pressure is the pressure that must be exceeded by the work of the left ventricle to open the aortic valve and result in ventricular ejection. Therefore, the increased volume work required to eject the additional blood (which flowed into the left ventricle across the incompetent aortic valve during diastole) is reduced because the work can be performed against a lower outflow impedance (lower diastolic pressure). Stroke volume and ejection fraction, therefore, may be preserved until late in the disease process. As with aortic stenosis, the presence of a competent mitral valve confines the changes to the left ventricle. However, the left ventricular dilation that follows chronic aortic insufficiency may result in mitral annular dilation or alteration in chordae tendineae geometry with resultant mitral regurgitation. Left atrial enlargement secondary to mitral regurgitation can therefore occur. It may also occur because of left atrial pressure overload as left ventricular end-diastolic pressures (LVEDPs) rise in the course of aortic insufficiency.

Mitral stenosis results in a chronically underfilled left ventricle because of progressive obstruction to left atrial emptying. This chronic underloading condition can result in decreased left ventricular thickness and diminished contractile function (a "disuse atrophy" of sort). In addition, if the cause of the mitral stenosis is rheumatic, myofibril damage may have occurred. Although the left ventricle is pressure and volume *under*loaded, the left atrium is both pressure and volume *over*loaded. To maintain flow across the progressively narrowing mitral orifice, the pressure in the left atrium must be correspondingly increasing. Gorlin's equation for pressure gradient follows.

$$\text{Pressure gradient} = \left\{\frac{\text{Flow rate}}{(\text{K} \times \text{valve area})}\right\}^2$$

It would predict that the pressure gradient increases by the square of any increase in flow rate or decrease in valve area. The elevations in left atrial pressure leads to hypertrophy and eventually dilation that predisposes to premature atrial contractions and subsequently atrial fibrillation. The loss of atrial contraction further diminishes forward flow across the stenotic mitral valve. The elevations in left atrial pressure limit pulmonary venous flow with consequent pulmonary engorgement. The pulmonary vasculature undergoes reactive changes, including intimal fibroelastosis inducing irreversible elevations in pulmonary vascular resistance. Right ventricular failure may develop because this chamber is poorly equipped to deal with the elevations in afterload (e.g., pulmonary hypertension).

Right ventricular dilation combined with increased right ventricular systolic pressures leads to tricuspid regurgitation.

Mitral regurgitation results in volume overload of the left ventricle. The outflow of the left ventricle is divided between the high-pressure/low-compliance outflow tract of the arterial tree and the low-pressure/high-compliance outflow route across the incompetent mitral valve into the left atrium. Although the volume work of the left ventricle is increased, the high-compliance outflow route permits a large portion of this work to be performed at a low pressure; therefore, left ventricular wall tension is minimally increased, if increased at all. As with aortic insufficiency, the volume overload results in marked left ventricular dilation and eccentric hypertrophy. In contrast, however, the left atrium is also volume overloaded and undergoes dilation. When the volume overload occurs slowly, the left atrium enlarges and minimal rises in pulmonary pressures result despite large regurgitant volumes. In contrast, the occurrence of acute mitral regurgitation, for example, an acute myocardial infarction with papillary muscle rupture, presents the left atrium with a sudden volume overload. Without the time to dilate, the left atrial pressure rapidly rises, limiting pulmonary drainage with resultant pulmonary engorgement.

Frogel J, Galusca D. Anesthetic considerations for patients with advanced valvular heart disease undergoing noncardiac surgery. *Anesthesiology Clin.* 2010;28:67–85.

Hartman GS. *Management of Patients with Valvular Heart Disease*. Cleveland: International Anesthesia Research Society; 1994:141–151. 1994 IARS Review Course Lectures.

Schoen FJ. Cardiac valves and valvular pathology: update on function, disease, repair, and replacement. *Cardiovasc Pathol.* 2005;14:189–194.

Thys DM, Hillel Z, Schwartz AJ, eds. *Textbook of Cardiothoracic Anesthesiology*. New York: McGraw-Hill; 2001:589–629.

Zipes DP, Libby P, Bonow RO, et al. eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 7th ed. Philadelphia: WB Saunders; 2005:1553–1615.

A.3. What are pressure–volume (P–V) loops? What do the different inflection points represent?

The P–V loop analysis (Fig. 6.1) depicts the relation between left ventricular volume and left ventricular pressure during a single cardiac cycle. Opening and closing of the mitral and aortic valves are represented by the inflection points A, B, C, and D, respectively (Fig. 6.1). Moving from points A through D, AB depicts left ventricular filling, BC depicts isovolumetric contraction, CD shows left ventricular ejection, and DA shows isovolumetric relaxation. Point A coincides with opening of the mitral valve and represents left ventricular end-systolic volume and early diastolic pressure. Point B is closure of the mitral valve and the end of diastolic pressure (LVEDP) and volume (left ventricular end-diastolic volume [LVEDV]). Point C represents the opening of the aortic valve and coincides with systemic, aortic diastolic pressure. Finally, point D is the closure of the aortic valve and represents left ventricular end-systolic pressure and volume, coinciding with the dicrotic notch in the aortic pressure tracing (Fig. 6.1). Left ventricular compliance is the relation between the change in pressure and change in volume of the chamber and is defined by the slope of the filling phase or segment AB. Preload is the P–V relation before the onset of contraction (LVEDP). Contractility may be illustrated by the slope of a line termed the *end-systolic pressure–volume relation* (ESPVR). The ESPVR slope is created by connecting multiple points (D) from multiple P–V loops generated by changing the filling volume to the left ventricle (LV) (Fig. 6.2). Increased contractility results in a steeper line, whereas diminished contractility results in a flatter relation. The P–V loop analysis permits illustration of stroke volume and ejection fraction. Stroke

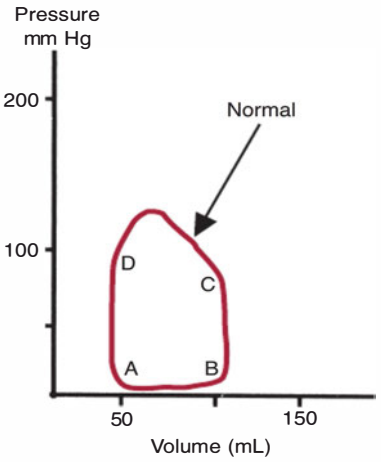


Figure 6.1 Normal pressure–volume loop and valve positions. *A.* Mitral valve (MV) opening. *B.* MV closure. *C.* Aortic valve (AV) opening. *D.* AV closure. *AB.* Left ventricular filling. *BC.* Isovolumetric contraction. *CD,* Ejection. *DA,* Isovolumetric relaxation.

volume is defined as difference in volume from the end of filling to the end of ejection (EDV–ESV), whereas the ejection fraction is the ratio of stroke volume to total volume in the heart at peak filling (SV/EDV). Therefore, the P–V loop analysis permits illustration of the volume–pressure relations and their changes with each of the four valvular lesions.

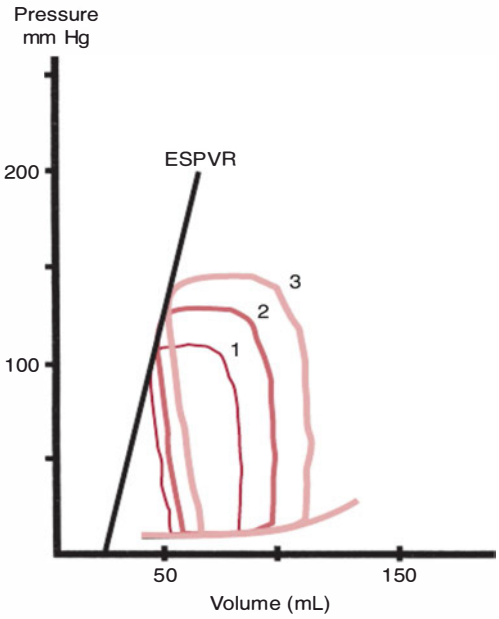


Figure 6.2 Contractility. ESPVR, end-systolic pressure–volume relations.

Hartman GS. *Management of Patients with Valvular Heart Disease.* Cleveland: International Anesthesia Research Society; 1994:141–151. 1994 IARS Review Course Lectures.

Sagawa K, Maugan L, Suga H, et al. *Cardiac contraction and the pressure-volume relationship.* New York: Oxford University Press; 1988.

Thomas SJ, Kramer JL, eds. *Manual of Cardiac Anesthesia.* 2nd ed. New York: Churchill Livingstone; 1993:81–127.

A.4. What are representative P–V loops for the four valvular lesions?

The hallmarks of aortic stenosis illustrated by the P–V loop analysis framework are a high left-ventricular systolic pressure and an upward and counterclockwise rotation in the end-diastolic P–V relation (AB) indicative of decreased chamber compliance (Fig. 6.3). Stroke volume and ejection fraction are well preserved, but the ejection phase of the loop occurs at much higher pressures. This is permitted by an increase in contractility of a counterclockwise rotation of the ESPVR line.

The schematic P–V loop for aortic insufficiency depicts the enlarged left ventricle of chronic aortic insufficiency. The minimal change in LVEDP despite the large volume overload is seen by the shift in the diastolic P–V curve to the right (A′B′) (Fig. 6.4). Low systemic diastolic pressures result in a brief isovolumetric phase (B′C′) and early complete ejection. The isovolumetric relaxation phase is absent because the incompetent valve permits regurgitant filling of the left ventricle from the aorta during diastole even before opening of the mitral valve. In contrast, when acute aortic insufficiency occurs, the left ventricular compliance is unchanged. Rapid increases in LVEDP from volume overload along the unshifted left ventricular diastolic P–V curve (AB) rapidly lead to increased left atrial pressure and pulmonary congestion.

The P–V loop of mitral stenosis illustrates hypovolemia, the cause of which cannot be determined from the loop alone (Fig. 6.5). Because the predominant impact of mitral stenosis occurs proximal to the left ventricle, the P–V analysis format is less useful.

In mitral regurgitation, the diastolic P–V relation (line AB) is shifted to the right, as it is in chronic aortic insufficiency, consistent with a marked increase in

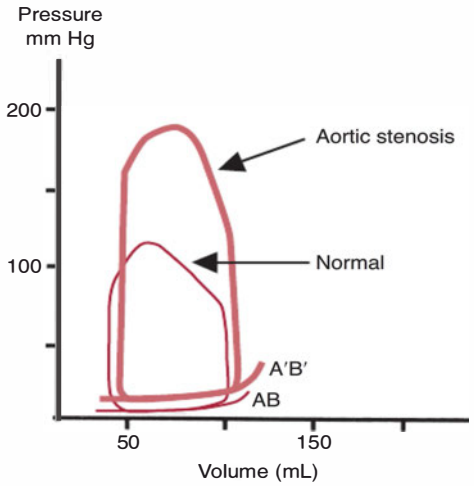


Figure 6.3 Pressure–volume loop of aortic stenosis.

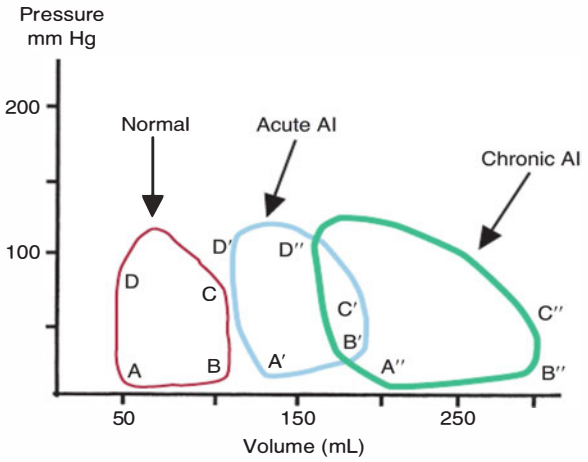


Figure 6.4 Pressure–volume loops of acute and chronic aortic insufficiency.

compliance (Fig. 6.6). The isovolumetric phase (BC) is nearly absent because the left atrium generally serves as a low-pressure/high-compliance route for ejection because of the incompetent mitral valve. Decreases in contractility are depicted by a decrease in the slope of the end-systolic-PV line (line through D). Nevertheless stroke volume and ejection fraction are maintained because of this low-pressure left atrial vent.

Hartman GS. *Management of Patients with Valvular Heart Disease*. Cleveland: International Anesthesia Research Society; 1994:141–151. 1994 IARS Review Course Lectures.

Sagawa K, Maugan L, Suga H, et al. *Cardiac Contraction and the Pressure-Volume Relationship*. New York: Oxford University Press; 1988.

Thomas SJ, Kramer JL, eds. *Manual of Cardiac Anesthesia*, 2nd ed. New York: Churchill Livingstone; 1993:81–127.

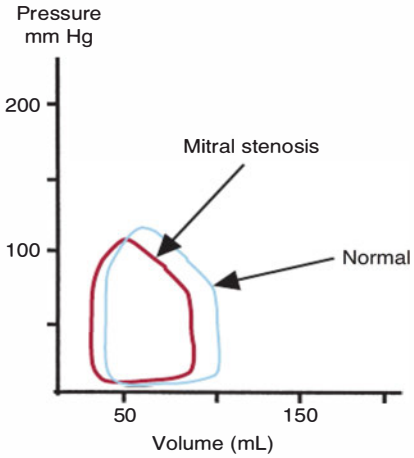


Figure 6.5 Pressure–volume loops of mitral stenosis.

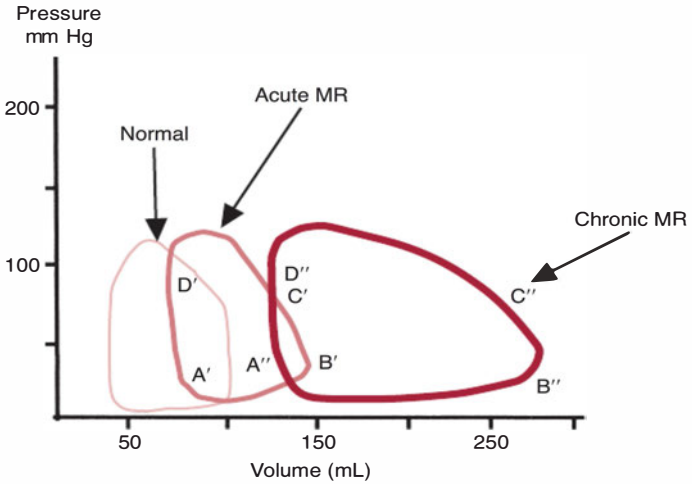


Figure 6.6 Pressure–volume loop of acute and chronic mitral regurgitation.

A.5. Draw the pressure/time curves for the left ventricle, left atrium, pulmonary artery, and aorta for a normal patient and for patients with each of the four valvular lesions.

Normal curves are shown in Fig. 6.7. The points A, B, C, and D correspond to the same points in the P–V loops.

Aortic Stenosis

The additional systolic pressure work of aortic stenosis can be seen in the left ventricular pressure tracing (Fig. 6.8). Elevations in LVEDP (point B) can be seen to diminish the perfusion gradient for coronary flow to the left ventricle. The augmentation in left ventricular filling late in diastole secondary to atrial contraction (left atrial "kick" from sinus rhythm) is highlighted in the inset. Rising left ventricular diastolic pressures secondary to decreased compliance necessitate elevations in left atrial pressures to permit complete left ventricular volume loading. Atrial systole provides this elevation in left atrial pressure synchronous with elevations in LVEDP while keeping left atrial pressures relatively low during the remaining cardiac cycle facilitating pulmonary venous drainage.

Aortic Insufficiency

The rapid upstroke and rapid decline of arterial pressure indicate absence of aortic valve closure and low end-diastolic aortic pressure (Fig. 6.9). Elevations in LVEDV and LVEDP are typical of aortic insufficiency. The early increase in LVEDP can result in left ventricular pressures exceeding those of the left atrium during diastole, with resultant premature closure of the mitral valve.

Mitral Stenosis

Elevations in pressure are seen in both the left atrial and pulmonary artery tracing with mitral stenosis (Fig. 6.10). The large gradient between left atrial and left ventricular pressures is highlighted in the inset. Chronic elevation in pulmonary volume induces changes in the luminary vascular bed and leads to pulmonary hypertension.

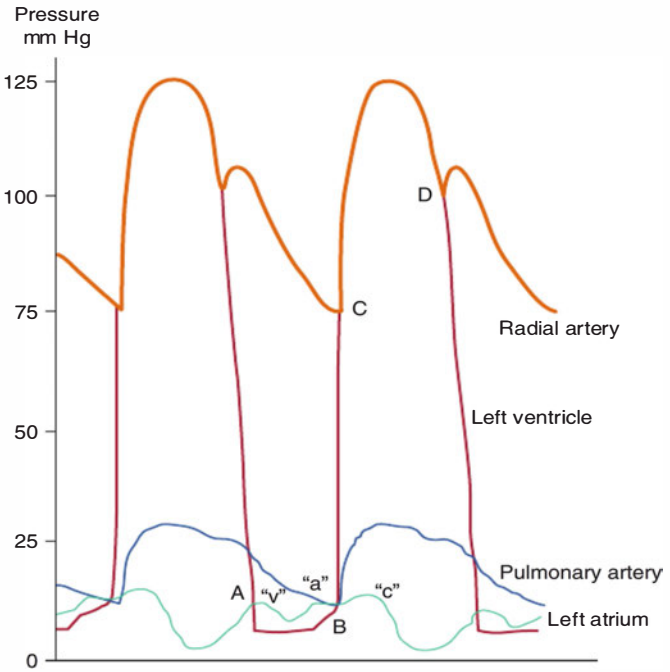


Figure 6.7. Pressure curves for the left ventricle, left atrium, pulmonary artery, and aorta in a healthy individual.

Mitral Regurgitation

The hallmark of mitral regurgitation is the marked elevations of left atrial pressure during systole and the occurrence of a giant "cv" wave and elevated pulmonary artery pressures (Fig. 6.11).

Hartman GS. *Management of Patients with Valvular Heart Disease.* Cleveland: International Anesthesia Research Society; 1994:141–151. 1994 IARS Review Course Lectures.

Kaplan JA, Reich DL, Konstadt SN, eds. *Cardiac Anesthesia.* 4th ed. Philadelphia: WB Saunders; 1999:727–784.

A.6. What are the basic principles of echocardiography? What are M-mode, B-mode, and Doppler color modalities? How do TTE and transesophageal echocardiography (TEE) differ?

Echocardiography is the use of sound waves to image structures and blood flow within the heart and great vessels. To image tissue, sound waves are emitted from a transducer at known speeds and constant intervals. The sound packets bounce off structures in their path, and the reflected sound waves are received at the point of origin, either by a separate receiving crystal or by the same emitting transducer, which spends a portion of its time in this "listening" mode. The time it takes for the reflected waves to return to the crystal is measured, and because the velocity of sound in tissues is relatively constant, solving for distance can be easily accomplished.

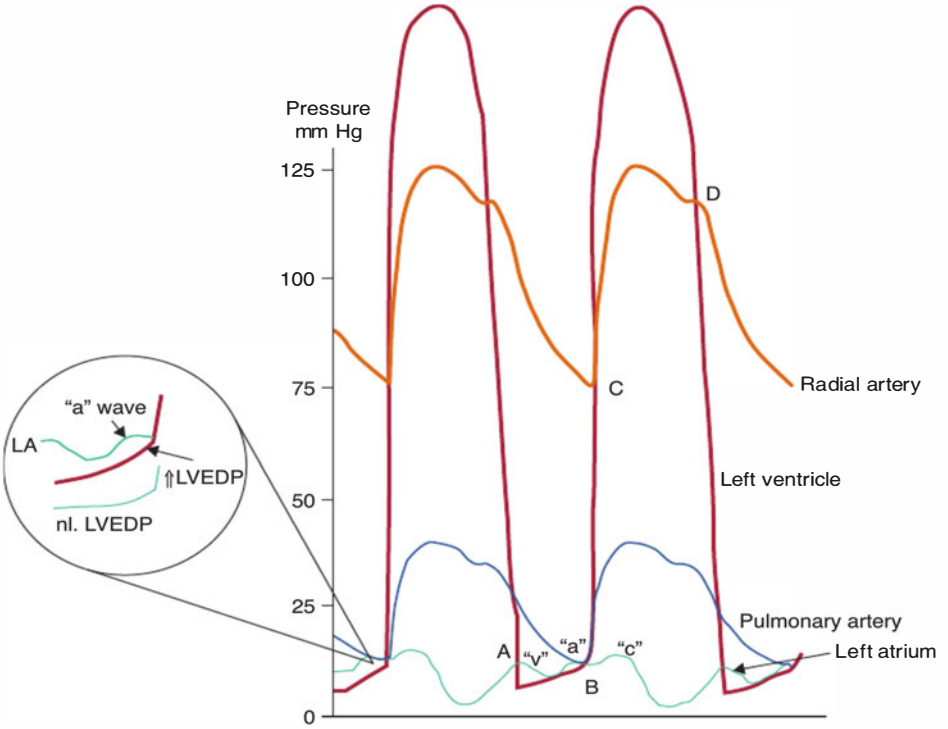


Figure 6.8 Pressure curves for the left ventricle, left atrium (LA), pulmonary artery, and aorta in patients with aortic stenosis. LVEDP, left ventricular end-diastolic pressure.

$$\text{Distance} = \tfrac{1}{2}\,(\text{velocity} \times \text{time})$$

(½ because the distance is traversed twice, once to the object and again on returning.)

In this manner, the spatial orientation of cardiac structures can be determined. The strength of the returning signal can be quantified as an amplitude, therefore "A" or amplitude mode (Fig. 6.12B). The echo machine codes this amplitude on a black and white scale, thereby converting the amplitude to brightness or B-mode scanning (Fig. 6.12C). Fig. 6.12D shows this "ice-pick" view through the left ventricle of the heart. Each change in tissue density results in some sound waves being reflected and hence an interface. In this example, bold lines are seen at the epicardial, the endocardial-chamber, the chamber-endocardial, and the epicardial borders. If these amplitude bars are displayed in real time, a motion or M-mode display results (Fig. 6.12E). These images were difficult to reliably obtain and interpret because the views represent a linear slice without surrounding structural images for referencing. If the probe is rocked back and forth repetitively, multiple M-mode images can be obtained in a given instant and a 2D image formed. This rapid rocking back and forth of the ultrasound beam is performed electronically in a phased-array transducer. The images derived in this manner appear as a cine-radiographic display of myocardial movement. Therefore, echocardiography can provide information about the size, shape, location, and movement of myocardial structures.

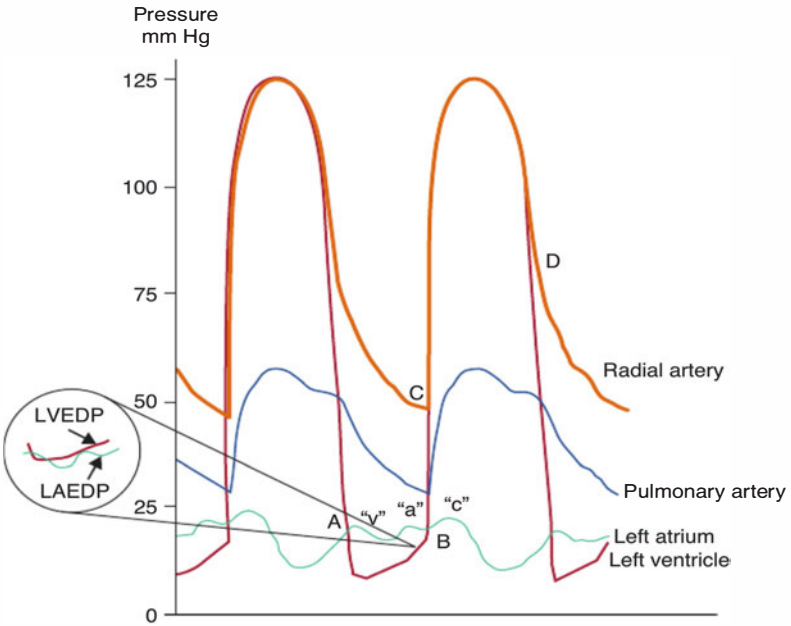


Figure 6.9 Pressure curves for the left ventricle, left atrium, pulmonary artery, and aorta in patients with aortic regurgitation. LAEDP, left atrium end-diastolic pressure; LVEDP, left ventricular end-diastolic pressure.

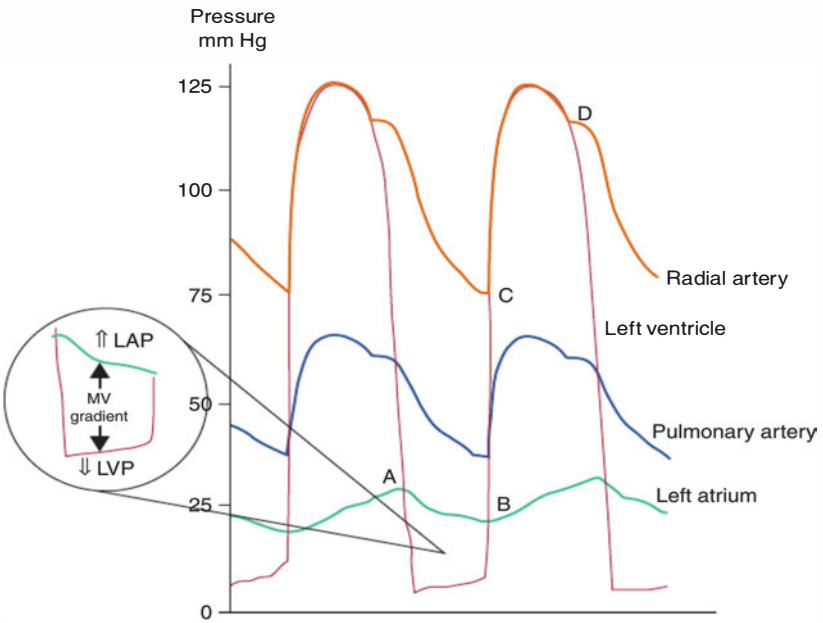


Figure 6.10 Pressure curves for the left ventricle, left atrium, pulmonary artery, and aorta in patients with mitral stenosis. LAP, left atrial pressure; LVP, left ventricular pressure; MV, mitral valve.

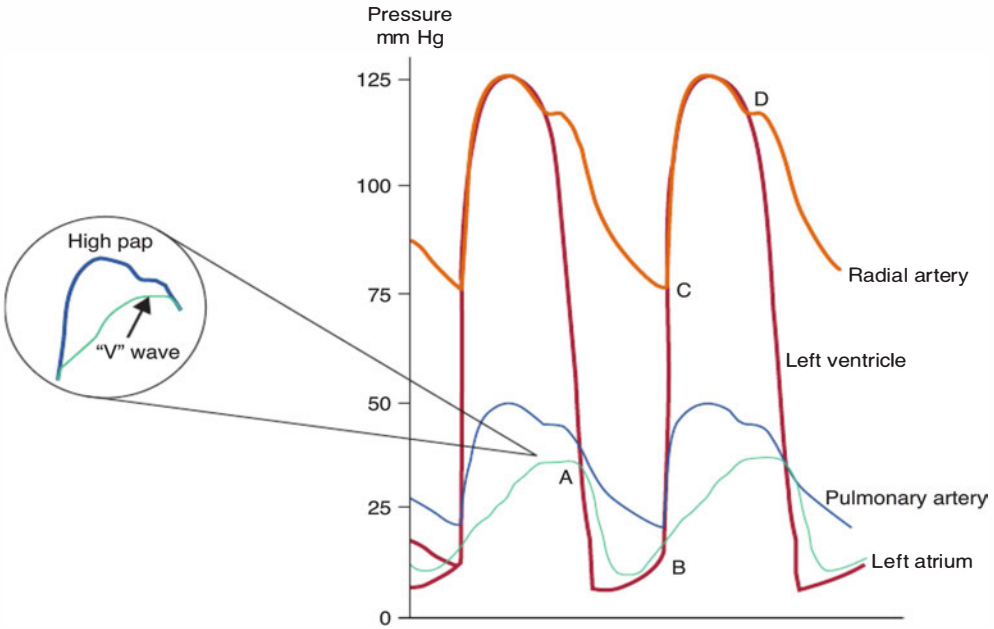


Figure 6.11 Pressure curves for the left ventricle, left atrium, pulmonary artery, and aorta in patients with mitral regurgitation. PAP, pulmonary artery pressure.

In addition to determining how long it takes for a given sound wave to return and thereby deriving the distance from the transducer, contact of the sound wave packet with the reflecting object (tissue, blood cells, air) will alter the wavelength of the sound packet according to the Doppler principle. When the object coming in contact with the sound wave is moving toward the source of the ultrasound, the reflected ultrasound wavelengths are compressed (shorter) or of higher pitch. The opposite occurs when the contacted object is moving away from the sound source. These shifts in frequency are proportional to the velocity of the contacted structure and, thereby, the speed and direction of the encountered object (usually of blood flow) can be calculated. This velocity information can be displayed on a color map (Doppler color flow) or on a time/velocity scale (spectral Doppler display). Doppler-derived blood flow velocity information can determine laminar and turbulent flow patterns, regurgitant or stenotic lesions, and congenital anomalies and can permit quantification of pressure gradients. Using the modified Bernoulli equation ($\delta P = 4\ v^2$), determination of a blood flow velocity permits the estimation of pressure gradients.

Simply, the greater the velocity of blood flow, the higher is the pressure gradient. Only the component of blood flow parallel to the Doppler beam will be analyzed. The Doppler equation: $V = c\ (F_S - F_T)/2\ F_T\ (\cos\ \theta)$, contains the cosine of the angle of incidence between the ultrasound beam and the moving object. Because the cosine of 90 degrees is zero, blood flow that is perpendicular to the ultrasound beam will not have any Doppler shift and, therefore, will not be represented in the color display. For this reason, it is important to choose an ultrasound "window" in which the expected blood flow direction is most parallel to the ultrasound.

TTE uses imaging points or "acoustic windows" obtained with the transducer handheld on the chest wall. It is simple and noninvasive. Most standard echocardiograms are obtained from this position. During cardiac surgery, the chest wall is in the sterile field and therefore unavailable. The esophagus lies immediately adjacent

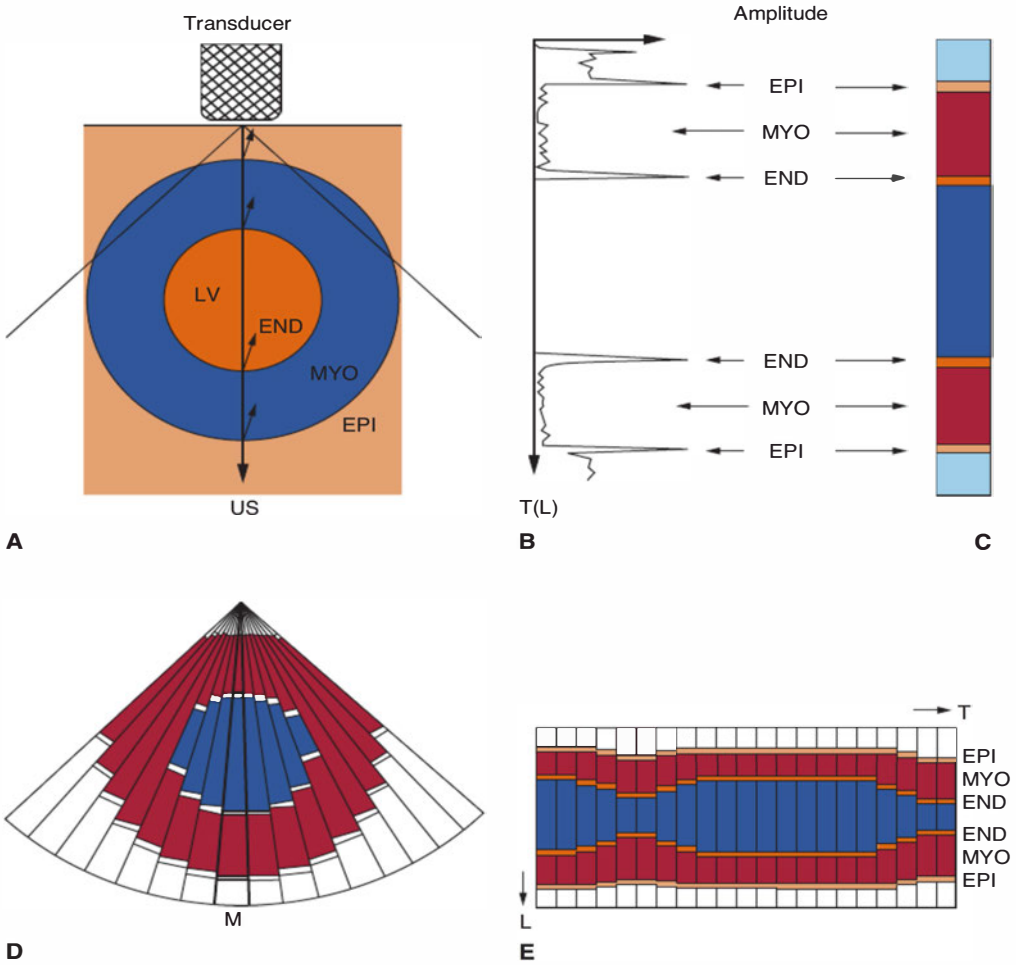


Figure 6.12 The process of producing the B-mode and M-mode images. **A.** A pulse of ultrasound is emitted into the object, and the backscattered echo is received by the same transducer. **B.** The received acoustic signal is converted to the electric signal (A-mode). **C.** The amplitude is modulated into brightness (B-mode). **D.** As subsequent pulses of ultrasound are emitted with the sequentially changing angles and the obtained one-dimensional (1D) B-mode images are compounded according to the direction of each ultrasound emission, the first frame of the sector-shaped image is formed. **E.** When the ultrasound is repeatedly transmitted in one direction, a series of 1D B-mode images is obtained. As these are arranged against time, an M-mode image is obtained. (From Okay Y, Goldiner PL, eds. *Transesophageal Echocardiography*. Philadelphia: JB Lippincott, 1992:12, with permission.) END, endocardium; EPI, epicardium; L, length; LV, left ventricle; M, motion; MYO, myocardium; T, time; US, ultrasound.

to the heart outside of the operative field and affords an excellent imaging vantage point. In 1976, Yasu Oka from the Albert Einstein College of Medicine developed a practical method of intraoperative imaging. He mounted an ultrasound crystal on the end of a gastroscope and, thereby, obtained images of the heart during surgery. This has been refined considerably since. TEE has become the standard of care for heart surgery at many institutions. The close proximity of the probe to the heart affords

excellent resolution. The probe is not in the operative field, so surgery is unhindered and sterility is not an issue. Although mildly invasive, the risk for esophageal injury in the anesthetized state is very low.

Intraoperative TEE is beneficial for quantification of cardiac contractility, for determination of the severity of regurgitant and stenotic valvular disease, for detection of intracardiac shunts and the occurrence of dissections, and as a guide for catheter placement.

Perrino AC, Reeves ST, eds. *A Practical Approach to Transesophageal Echocardiography*. Philadelphia: Lippincott Williams & Wilkins; 2003:3–94.

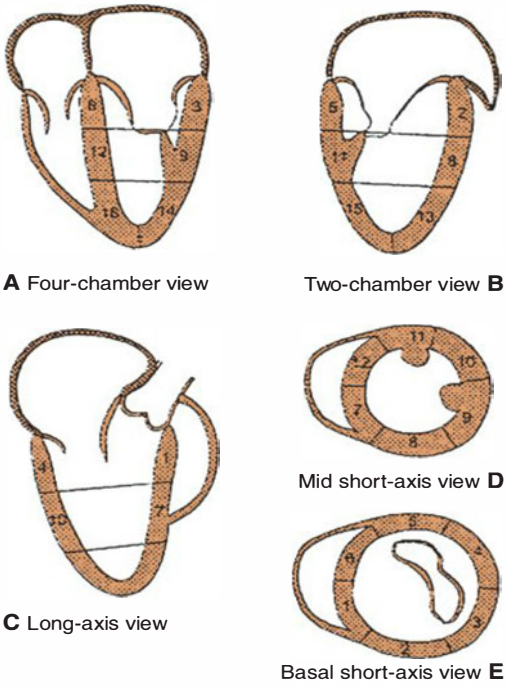
Savage RM, Aronson S, eds. *Comprehensive Textbook of Intraoperative Transesophageal Echocardiography*. Philadelphia: Lippincott Williams & Wilkins; 2005:3–61.

A.7. What are the three TEE vantage points for the comprehensive imaging of the left ventricle? How are pressure gradients measured by echocardiography? How do the pressure gradients derived from Doppler echocardiography differ from those obtained in the catheterization laboratory by direct pressure measurement?

The heart has two main axes: the longitudinal axis running from the base to the apex and the short axis perpendicular to that. Because the ultrasound beam can be thought of as a 2D structure, multiple scan planes are required to completely image a 3D structure. The left ventricle may be divided into 16 segments: 6 at the basal level, 6 at the midpapillary level, and 4 at the apical level (Fig. 6.13). By moving the transesophageal echocardiography probe in the esophagus and rotation of the crystal within the transducer tip, the left ventricle can be imaged from three acoustic windows. These are the midesophageal four-chamber, the transgastric short axis, and the transgastric two-chamber view. Normal ventricular motion requires that the wall segment move centrally with systole and similarly undergo thickening along this axis during contraction. Function is usually quantified as normal; mild, moderate, and severe hypokinesis; akinesis; and dyskinesis.

In addition to function, TEE permits the determination of wall thickness and chamber size—important parameters in understanding the pathophysiology of valvular heart disease.

As mentioned previously, pressure gradients are derived through analysis of the Doppler profiles of blood flow. A commonly determined echocardiography gradient is that which is present from the left ventricle to the aorta in the setting of aortic stenosis. To obtain the change in blood flow velocity across the aortic valve with TEE, the probe is advanced far into the stomach and sharply anteflexed and left deflected to obtain the window from the apex of the heart (deep transgastric long axis) and align the ultrasound beam most parallel to the path of blood flow. From this window, the continuous-wave Doppler cursor is directed across the left ventricular outflow tract and aortic valve. An example of such a spectral Doppler display is seen in Figure 6.14. The large increase in blood flow velocity in this display occurs at the narrowest point along its path, which, in this case, is the aortic valve. Using the modified Bernoulli equation mentioned previously, a gradient is calculated (100 mm Hg in the example). This represents the maximum instantaneous pressure difference between the left ventricle and the aorta. Aortic stenosis is also quantified at the time of catheterization by measuring the pressures from within the left ventricle and the aorta as a rapid response pressure transducer catheter is withdrawn from the left ventricle back to the aorta across the stenotic valve. The standard reported gradient is the difference between the maximum left ventricular and aorta pressures. Figure 6.15 illustrates that these peaks are not simultaneous events. Therefore, Doppler-derived aortic stenosis gradients are usually higher than those derived at the time of left heart catheterization.



Basal segments	Mid segments	Apical segments
1 = Basal anteroseptal	7 = Mid anteroseptal	13 = Apical anterior
2 = Basal anterior	8 = Mid anterior	14 = Apical lateral
3 = Basal lateral	9 = Mid lateral	15 = Apical inferior
4 = Basal posterior	10 = Mid posterior	16 = Apical septal
5 = Basal inferior	11 = Mid inferior	
6 = Basal septal	12 = Mid septal	

Figure 6.13 Sixteen-segment model of the left ventricle. **A.** Four-chamber views show the three septal and three lateral segments. **B.** Two-chamber views show the three anterior and three inferior segments. **C.** Long-axis views show the two anteroseptal and two posterior segments. **D.** Mid–short-axis views show all six segments at the mid level. **E.** Basal short-axis views show all six segments at the basal level. (From Shanewise JS, Cheung AT, Aronson S, et al, eds. ASE/SCA guidelines for performing a comprehensive intraoperative multiplane transesophageal echocardiography examination: recommendations of the American Society of Echocardiography council for intraoperative echocardiography and the Society of Cardiovascular Anesthesiologists task force for certification in perioperative transesophageal echocardiography. Anesth Analg. 1999;89:870–884, with permission.)

Perrino AC, Reeves ST, eds. *A Practical Approach to Transesophageal Echocardiography*. Philadelphia: Lippincott Williams & Wilkins; 2003:77–130.

Savage RM, Aronson S, eds. *Comprehensive Textbook of Intraoperative Transesophageal Echocardiography*. Philadelphia: Lippincott Williams & Wilkins; 2005:65–102.

Shanewise JS, Cheung AT, Aronson S, et al. ASE/SCA guidelines for performing a comprehensive multiplane transesophageal echocardiography examination: recommendations of the American Society of Echocardiography and the Society of Cardiovascular Anesthesiologists task force for certification in perioperative transesophageal echocardiography. *Anesth Analg.* 1999;89:870–884.

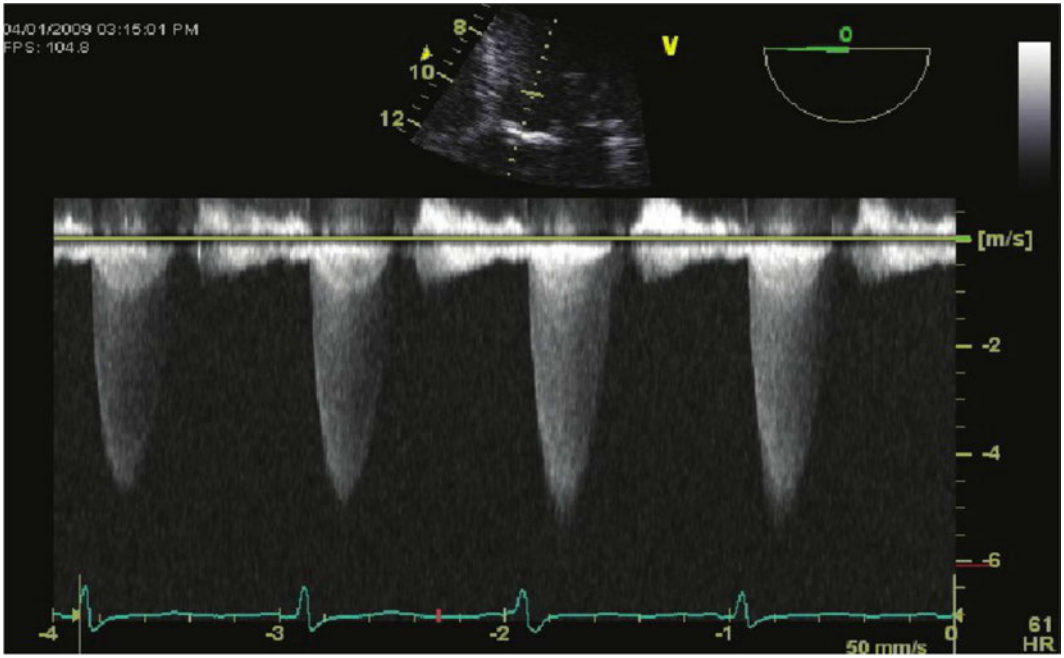


Figure 6.14 Continuous-wave Doppler across the aortic valve in the deep transgastric apical view from a patient with severe aortic stenosis.

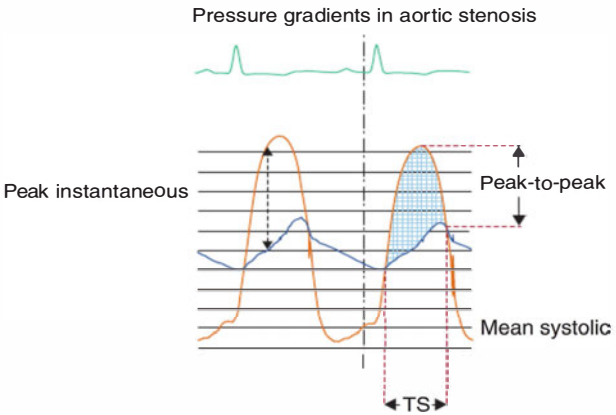


Figure 6.15 Pressure gradients in severe aortic stenosis are measured during systole as the difference between aortic and left ventricular pressures displayed using a scale of 0 to 20 mm Hg. The peak instantaneous gradient is the maximum gradient noted; the peak-to-peak gradient is the difference between peak left ventricular and aortic pressures. The mean systolic gradient is the average of all systolic pressure gradients noted during systolic ejection (TS). (Adapted from Nanda NC, ed. *Doppler Echocardiography.* Philadelphia: Lea & Febiger; 1993:130.)

A.8 What is the role for three-dimensional (3D) echocardiography in the operating room?

Modern TEE technology has progressed from 2D multiplane images to real-time 3D displays of the heart. The 3D probes are equipped with 20 to 40 times more piezoelectric crystals on the same size probe surface. This allows for a pyramidal scanning volume.

The orientation of the mitral valve is such that perpendicular alignment of the TEE probe is achieved. All of the 3D imaging modalities can be used to assess valvular pathology (live, zoom, and full-volume). The MV 3D images can be further modified by cropping in any plane to investigate leaflet morphology. Studies have shown that intraoperative assessment of the mitral valve with 3D TEE examinations have decreased interobserver variability and provided better correlation with surgical findings.

The atrial valve is more difficult to image in 3D. A normal atrial valve with thin cusps are not well visualized. Stenotic valves encounter echo dropout secondary to calcifications.

Left ventricular assessments including volume and wall motion can easily be done in the operating room. After identification of the left ventricle walls and apex from two orthogonal 2D views, a 3D model of the heart is created using endocardial border tracking. Stroke volume and ejection fraction are automatically calculated.

Jungwirth B, Mackensen G. Real-time 3–dimensional echocardiography in the operating room. *Semin Cardiothorac Vasc Anesth.* 2008;12:248–264.

Vegas A, Meineri M. Three-dimensional transesophageal echocardiography is a major advance for intraoperative clinical management of patients undergoing cardiac surgery: a core review. *Anesth Analg.* 2010;110:1548–1573.

A.9. What are the echocardiographic and cardiac catheterization criteria for the four valvular lesions?

The TEE severity scales of the various valvular lesions are summarized in Table 6.1.

Aortic Stenosis

Echocardiographic criteria for aortic stenosis include 2D images demonstrating limited aortic valve opening and motion and left ventricular concentric hypertrophy. Doppler examination will reveal a turbulent, high-velocity jet across the aortic valve, and color-flow Doppler will demonstrate a turbulent, mosaic-appearing color map. The gradient across the aortic valve measured at cardiac catheterization is different from that measured by echocardiography as mentioned previously. Quantification of this Doppler-derived pressure gradient again relies on the modified Bernoulli equation.

$$\text{Pressure gradient} = 4\ v^2$$

where v = velocity (m/second), pressure (mm Hg)

Because flow is an important determinant of pressure gradients, both the catheterization and Doppler-derived values are interpreted along with cardiac output. Calculations permit the determination of a valve area. Severe aortic stenosis is present when the gradient exceeds 75 mm Hg or the valve area is less than 0.8 cm^2.

Aortic Insufficiency

Catheterization criteria for aortic insufficiency rely on the qualitative estimation of the regurgitation volume and an estimation of left ventricular size and ejection fraction. Similar quantification can be made from Doppler color echocardiography-derived data. A commonly used echocardiographic criteria compares the width of the regurgitant jet at the level of the valve to the width of the left ventricular outflow tract. A ratio of greater than 0.66 corresponds with severe aortic insufficiency. Another sign

Table 6.1 Transesophageal Echocardiography Severity Scales of Valvular Lesions

	SEVERITY SCALES				
	NORMAL	MILD	MODERATE		SEVERE
MEASUREMENT	0	1+	2+	3+	4+
MS					
MVA (cm^2)	4.0–6.0	1.5–2.5	1.0–1.5		<1.0
Mean pressure gradient (mm Hg)	<2	2.0–6.0	6.0–12.0		>12
AS					
AVA (cm^2)	2.5–3.5	1.2–2.0	0.8–1.1		<0.8
Peak pressure gradient (mm Hg)	<10	16–34	35–75		>75
MR					
Jet length/LA length	0	<1/3	1/3–2/3		>2/3
Jet area/LA area	0	<1/3	1/3–2/3		>2/3
Jet area (cm^2)	0	<3	3.0–6.0		>6
Pulmonary vein Doppler	S wave ≫ D wave	Blunting S wave	S < D	S ≪ D	Systolic reversal of flow
AI					
Jet width/LVOT width	0	<1/4	1/4–1/2	1/2–2/3	>2/3
Jet length (pressure dependent)	0	To middle of AML	To tip of AML	To PM	Beyond PM

AI, aortic insufficiency; AML, anterior mitral leaflet; AS, aortic stenosis; AVA, aortic valve area; LA, left atrial; LVOT, left ventricular outflow tract; MR, mitral regurgitation; MS, mitral stenosis; MVA, mitral valve area; PM, papillary muscle.

of severe aortic insufficiency can be observed in the spectral Doppler display of blood velocity in the descending thoracic aorta. The TEE probe is advanced to the level of the descending thoracic aorta and rotated to 90 degrees to obtain a long axis view. Under normal conditions, flow remains forward (to distal beds) during diastole. In severe aortic insufficiency, regurgitation of blood back into the ventricle decreases proximal pressure in the aorta and thus the spectral display of blood velocities will demonstrate a reversal of blood flow during diastole back toward the aortic root.

Mitral Stenosis

The severity of mitral stenosis can be obtained by the direct measurement of a diastolic gradient between the left atrium and ventricle at the time of cardiac catheterization. This requires a transatrial puncture, a procedure largely replaced by echocardiographic techniques. Echocardiographic diagnosis is based on gradient estimation by Doppler and by measuring the rate of decay in the pressure with the time spent in diastole (pressure halftime). The mitral area in square centimeters can be derived from an empirical formula wherein the mitral valve area equals 220 divided by this pressure halftime (Hatle constant). Severe mitral stenosis is present when the end-diastolic gradient exceeds 12 mm Hg, corresponding to a valve area of less than 1.0 cm^2.

Mitral Regurgitation

In the presence of mitral regurgitation, ventriculography will demonstrate the reflux of dye from the left ventricle into the left atrium. Severe mitral regurgitation is diagnosed when dye refluxes into the pulmonary veins. Color Doppler echocardiography permits similar quantification. Estimation relies on an estimation of regurgitant jet volume as compared with the left atrium and through analysis of pulmonary venous flow profiles.

In every case, color Doppler echocardiography is often useful in identifying the cause of the valvular lesion, its extent of involvement within and around the valve, and the associated hemodynamic changes. Therefore, for many valvular lesions, it may be sufficient for the diagnosis. Catheterization, however, is often performed to assess the presence of concomitant coronary artery disease, especially in patients of advanced age.

Quinones M, Otto C, Stoddard M, et al. Recommendations for quantification of Doppler echocardiography: a report of from the Doppler quantification task force of the nomenclature and standard's committee of the American Society of Echocardiography. *J Am Soc Echocardiogr.* 2002;15:167–180.

Schoen FJ. Cardiac valves and valvular pathology: update on function, disease, repair, and replacement. *Cardiovasc Pathol.* 2005;14:189–194.

Weyman AE, ed. *Principles and Practice of Echocardiography*. 2nd ed. Philadelphia: Lea & Febiger; 1994:391–574.

Zipes DP, Libby P, Bonow RO, et al, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 7th ed. Philadelphia: WB Saunders; 2005:1553–1615.

B. Preoperative Evaluation and Preparation

B.1. What are the presenting signs and symptoms of the four valvular lesions listed previously?

See Table 6.2.

Aortic Stenosis

The triad of angina, syncope, and congestive heart failure represent the progression of symptoms associated with atrial stenosis. These symptoms correlate directly with mortality; the 50% survival data for these symptoms are 5, 3, and 2 years from the

Table 6.2 The Signs and Symptoms for the Various Valvular Lesions

LESION	SIGNS AND SYMPTOMS
AS	Angina, syncope, dyspnea/CHF
AI	
Chronic	Fatigability, dyspnea
Acute	Severe pulmonary edema, CHF
MS	Pulmonary congestion, AFib
MR	
Chronic	DOE, PND, AFib
Acute	Severe pulmonary edema, CHF

AFib, atrial fibrillation; AI, aortic insufficiency; AS, aortic stenosis; CHF, congestive heart failure; DOE, dyspnea on exertion; MR, mitral regurgitation; MS, mitral stenosis; PND, paroxysmal nocturnal dyspnea.

onset of these symptoms, respectively. Angina results from both increased demand for and a decrease in supply of coronary blood flow. Increased muscle mass from LVH and the high energy requirements to generate increased (high) systolic pressure combine to increase demands for coronary blood flow. In addition, insufficient supply secondary to decreased perfusion gradients and a decrease in coronary vasculature relative to the large amount of myocardium sum to diminish relative myocardial blood supply. Therefore, up to one-third of patients with aortic stenosis can have angina in the absence of significant coronary artery disease.

Aortic Insufficiency

Patients with aortic insufficiency have variable clinical presentations, primarily depending on the rapidity with which the left ventricular volume overload develops. When the volume increase occurs gradually as in chronic aortic insufficiency, there is usually a long asymptomatic period. The onset of the symptoms of fatigability and dyspnea signals either reduced cardiac output or increased LVEDP, indicative of impairment of left ventricular contractile function. When aortic insufficiency occurs acutely, the ventricular compliance is unchanged; increased left ventricular diastolic volumes from regurgitant flow, therefore, lead to rapid rises in LVEDP and the clinical picture of congestive failure.

Mitral Stenosis

Mitral stenosis is a slowly progressive obstruction to flow across the mitral valve with gradual increase in left atrial pressure and volume. Symptoms of pulmonary congestion result from elevations in left atrial pressures and *not* from poor left ventricular systolic function. Atrial fibrillation develops secondary to atrial dilation.

Mitral Regurgitation

The time course for the development of mitral regurgitation determines the severity of the symptoms. When the volume of regurgitant flow from the left ventricle to the left atrium increases gradually, the left atrium compensates by gradual dilatation. In contrast, the onset of acute mitral regurgitation can lead to rapid increases in left atrial pressures, severe pulmonary congestion, and congestive heart failure.

Frogel J, Galusca D. Anesthetic considerations for patients with advanced valvular heart disease undergoing noncardiac surgery. *Anesthesiology Clin.* 2010;28:67–85.

Hartman GS. *Management of Patients with Valvular Heart Disease.* Cleveland: International Anesthesia Research Society; 1994:141–151. 1994 IARS Review Course Lectures.

Thomas SJ, Kramer JL, eds. *Manual of Cardiac Anesthesia.* 2nd ed. New York: Churchill Livingstone; 1993:81–127.

Zipes DP, Libby P, Bonow RO, et al. eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine.* 7th ed. Philadelphia: WB Saunders; 2005:1553–1615.

B.2. What is the New York Heart Association classification of heart failure?

The New York Heart Association heart failure classification is based on the amount of symptoms, specifically dyspnea and fatigue. The various classes are listed in the following:

Class I. No symptoms
Class II. Symptoms with ordinary activity
Class III. Symptoms with less than ordinary activity
Class IV. Symptoms at rest

Criteria Committee of the New York Heart Association. *Diseases of the Heart and Blood Vessels (Nomenclature and Criteria for Diagnosis)*. 6th ed. Boston: Little, Brown and Company, 1964.

B.3. Discuss the role of premedication for patients with the four different valvular lesions.

The role of premedication is to allay the anxiety of the impending surgical procedure, thereby controlling the sympathetic outflow that may accompany the stress response. Acute changes in heart rate, venous return, and systemic resistance can have particularly profound effects on patients with valvular heart disease.

Patients with aortic stenosis may benefit from premedication by preventing unnecessary increases in heart rate. Concern must be taken to ensure adequate venous return and preservation of sinus mechanism (see later discussion).

Patients with aortic insufficiency can similarly benefit from premedication because any increases in afterload, which may accompany sympathetic stimulation, can increase regurgitant volume. Drug doses should be adjusted based on the severity of debilitation and degree of systemic hypoperfusion.

Patients with mitral stenosis should be premedicated with caution. Elevations in carbon dioxide resulting from narcotic-induced hypoventilation can dramatically elevate pulmonary pressures further compromising right ventricle output. Conversely, venodilation may excessively diminish filling pressures.

Patients with mitral regurgitation can respond similarly to those with mitral stenosis, particularly when pulmonary hypertension is present. However, elevations in systemic pressure from stress can also compromise forward left ventricular output. Proper premedication can be delivered by careful dose selection and the provision of supplemental oxygen.

Hartman GS. *Management of Patients with Valvular Heart Disease.* Cleveland: International Anesthesia Research Society; 1994:141–151. 1994 IARS Review Course Lectures.

Thomas SJ, Kramer JL, eds. *Manual of Cardiac Anesthesia.* 2nd ed. New York: Churchill-Livingstone; 1993:81–127.

B.4. How would you premedicate the patient with severe atrial stenosis and mitral regurgitation?

Premedication of a patient with severe atrial stenosis and mitral regurgitation must be approached with caution. The patient should receive supplemental oxygen. A light premedication could be provided with small doses of benzodiazepines by mouth. However, I would prefer to titrate in small intravenous doses of sedation while the patient was under the closely monitored situation of the operating room or holding area and with inspired oxygen supplementation. In this setting, incremental doses of midazolam 0.5 mg intravenously would be administered. It is important to remember that there may be significant delay in the onset of effect of intravenous medications secondary to pooling in the pulmonary and left atrial systems. Adequate waiting periods must be observed between each aliquot to avoid inadvertent overdose with ensuing respiratory depression, pulmonary hypertension, systemic hypotension, and right heart failure. In the elderly, use of benzodiazepines has been linked to postoperative delirium, which can be quite severe and difficult to treat as well as increase length of stay and resource utilization.

C. Intraoperative Management

C.1. Outline the hemodynamic management goals for each of the four valvular lesions. What are the anesthetic goals with respect to heart rate and rhythm, preload, afterload, and contractility?

Table 6.3 summarizes the hemodynamic goals with respect to heart rate and rhythm, preload, afterload, and contractility.

Table 6.3 Hemodynamic Goals for the Various Valvular Lesions

		HEMODYNAMIC GOALS		
LESIONS	HR AND RHYTHM	PRELOAD	AFTERLOAD	CONTRACTILITY
AS	60–70, sinus	Full	Maintain	—
AI	80–90	Maintain	Lower	May need support
MS	60–70	Full	—	—
MR	80–90, sinus if possible	Maintain	Lower	May need support

AI, aortic insufficiency; AS, aortic stenosis; HR, heart rate (beats/min); MR, mitral regurgitation; MS, mitral stenosis.

Aortic Stenosis

Patients with aortic stenosis need the left ventricular filling obtained through a well-timed atrial contraction. Similarly, LVH renders the ventricle stiff and adequate preload is required. Reducing vascular tone will do little to relieve the fixed afterload increases from a stenotic valve but rather lower diastolic coronary perfusion gradients and should be avoided. Patients with aortic stenosis experiencing angina may require the administration of an α-agonist such as phenylephrine rather than nitroglycerin to increase coronary perfusion pressure.

Aortic Insufficiency

The severity of aortic insufficiency is determined by the size of the regurgitant orifice, the pressure gradient between the aorta and left ventricle during diastole, and the time spent in that phase of the cardiac cycle. Elevated heart rates decrease the time spent in diastole and can lead to a decrease in heart size. Afterload reduction can lessen the regurgitant driving forces, but therapeutic maneuvers to accomplish this may be limited by resulting systemic hypotension.

Mitral Stenosis

Patients with mitral stenosis can swiftly deteriorate in the setting of rapid heart rates. The decreased filling time necessitates the marked elevation of left atrial pressures, and pulmonary edema can rapidly ensue. Whereas left ventricle contractility is generally preserve in mitral stenosis, use of β-blockade does result in decreased right ventricular contractility, which in the setting of pulmonary hypertension can further compromise the cardiac output and systemic blood pressure. However, the loss in right ventricle contractility is more than offset by the beneficial effects of the reduction of heart rate. Slower heart rates permit adequate time for transfer of blood from the left atrium to the left ventricle across the stenotic mitral valve to occur. In addition, the pressure gradient across the mitral valve is also reduced; thereby lowering left atrial pressure and diminishing pulmonary congestion. Because there is some variability in the individual response, the use of short-acting β-blockers such as esmolol is prudent because an adverse response should be evanescent.

Mitral Regurgitation

Patients with mitral regurgitation can rapidly deteriorate with marked increases in systemic blood pressure and afterload. As with other volume overload lesions such as aortic insufficiency, slightly rapid heart rates (80 to 90 beats per minute) should result in smaller left ventricular volumes. This may lessen any component of mitral regurgitation secondary to annular dilation or chordal malalignment. Importantly, tachycardia should be avoided in patients with ischemic mitral regurgitation.

C.2. What are the hemodynamic goals for this patient with the combination of severe aortic stenosis and mitral regurgitation?

In the patient with combined aortic stenosis and mitral regurgitation, the situation is more complex than when only a singular valvular lesion is present. Careful examination of the hemodynamic goals for each of the two lesions will reveal that therapy beneficial to patients with atrial stenosis may exacerbate the severity of the mitral regurgitation. Early aggressive intervention is the key to these combined lesions. A lower margin for error usually exists because minor hemodynamic aberrations can rapidly lead to cardiac collapse. A good rule of thumb is to prioritize the management based on the character of the present symptoms. Patients with aortic stenosis and mitral regurgitation who present with syncope or angina are best managed for their atrial stenosis, whereas patients with dyspnea and pulmonary edema are best managed for their congestive symptoms. It is prudent to maintain the patient's own usual hemodynamics and avoid physiologic trespass. TEE evaluation of left ventricular performance can be helpful in separating pulmonary congestion secondary to left heart failure from that secondary to poor diastolic left ventricular compliance.

Frogel J, Galusca D. Anesthetic considerations for patients with advanced valvular heart disease undergoing noncardiac surgery. *Anesthesiology Clin.* 2010;28:67–85.

Hartman GS. *Management of Patients with Valvular Heart Disease.* Cleveland: International Anesthesia Research Society; 1994:141–151. 1994 IARS Review Course Lectures.

Thomas SJ, Kramer JL, eds. *Manual of Cardiac Anesthesia.* 2nd ed. New York: Churchill Livingstone; 1993:81–127.

C.3. How would you monitor this patient with severe atrial stenosis and mitral regurgitation?

In addition to the standard American Society of Anesthesiologists recommended monitors, the patient would have a radial artery and a pulmonary artery catheter. Following induction of anesthesia and endotracheal intubation, a TEE probe would be inserted to confirm the valvular pathology and to assess ventricular function. Following valve replacement, the TEE probe would be used to check for adequacy of valvular function and the absence of paravalvular leaks and to assess postbypass ventricular function.

Practice guidelines for perioperative transesophageal echocardiography. A report by the American Society of Anesthesiologists and the Society of Cardiovascular Anesthesiologist Task Force on transesophageal echocardiography. *Anesthesiology.* 1996;84:986–1006.

C.4. Should the patient have a pulmonary artery catheter placed before induction?

Volume status may be particularly difficult to assess in patients with valvular heart disease yet of critical importance in the management of these patients. Patients with stenotic lesions depend on adequate filling pressures for diastolic filling of the ventricle. Patients with the volume overload lesions of aortic insufficiency and mitral regurgitation can benefit from the careful reductions in pulmonary pressure guided by the simultaneous assessment of cardiac performance. In these capacities, the pulmonary artery catheter is useful. Patients with current hemodynamic stability, without severe respiratory distress, can be safely anesthetized before placement of the pulmonary artery catheter. In all, there is no evidence that use of the pulmonary artery catheter improves outcome in the setting of surgery.

Practice guidelines for pulmonary artery catheterization: an updated report by the American Society of Anesthesiologists task force on pulmonary artery catheterization. *Anesthesiology*. 2003;99:4.

C.5. Is a pulmonary artery catheter with pacing capabilities indicated?

Patients with aortic stenosis can become severely compromised with the loss of atrial kick or the presence of slow junctional rhythms. Patients with aortic insufficiency or mitral regurgitation can experience left ventricular dilation in the setting of slow heart rates. In such cases, a pulmonary artery catheter with atrial and ventricular pacing capacity can be useful in this setting. In patients with intact conduction systems, rate manipulation can often be achieved pharmacologically. Transesophageal atrial pacing is another option; transthoracic pacing elicits a ventricular response only and does not permit atrial stimulation. Transthoracic pacing is indicated when the ability to rapidly open the pericardium and obtain epicardial pacing is limited. This occurs in the setting of reoperations or with patients having a history of inflammatory pericardial disease. Pacing will be limited to capture of the ventricle alone. The loss of atrial contraction can lead to underfilling and hemodynamic compromise in patients dependent on the added volume from atrial systole. One of the other pacing modalities is best in this setting.

Maisel WH, Epstein AE. The role of cardiac pacing: American College of Chest Physicians guidelines for the prevention and management of postoperative atrial fibrillation after cardiac surgery. *Chest*. 2005;128(suppl 2):36S–38S.

Risk SC, Brandon D, D'Ambra M, et al. Indications for the use of pacing pulmonary artery catheters in cardiac surgery. *J Cardiothorac Vasc Anesth*. 1992;6:275–279.

C.6. What anesthetic technique would you employ? Why?

For the patient undergoing CPB and aortic valve replacement, general anesthesia with endotracheal intubation is the obvious choice. Both narcotics and inhalation anesthetics can be safely administered. When prolonged postoperative ventilation is anticipated, a high-dose narcotic anesthetic has numerous advantages. Recent anesthetic technique for cardiac surgery has focused on the use of techniques permitting earlier extubation, so-called fast tracking. Anesthetic combinations using smaller total narcotic doses, inhalation anesthetics, and short-acting intravenous sedatives such as propofol are gaining popularity. For uncomplicated valve replacements with good ventricular function, the advantages of early extubation can be safely achieved. In complicated cases with longer bypass periods, poor ventricular function, or postbypass bleeding, the hemodynamic stability of a high-dose narcotic technique may be advantageous.

DiNardo JA. *Anesthesia for Cardiac Surgery*. 2nd ed. Stamford, CT: Appleton & Lange; 1998:109–140.

Howie MB, Black HA, Romanelli VA, et al. A comparison of isoflurane versus fentanyl as primary anesthetics for mitral surgery. *Anesth Analg*. 1996;83:941–948.

Tuman KJ, McCarthy RJ, Spiess BD, et al. Comparison of anesthetic techniques in patients undergoing heart valve replacement. *J Cardiothorac Anesth*. 1990;4:159–167.

C.7. What muscle relaxant would you use for this patient?

Muscle relaxants can alter hemodynamics both from the effects of histamine release, including vasodilatation and bronchospasm, and through effects on rhythm. Although slowing of heart rates usually benefits the patient with angina, it may have

severe consequences in patients with valvular heart disease. The typical high-dose narcotic anesthesia usually results in bradycardia secondary to the vagotonic actions. Pancuronium-mediated increases in heart rate usually offset these actions and result in a stable heart rate.

Hemodynamically "neutral" relaxants such as vecuronium, rocuronium, or cisatracurium could be used, but their intermediate duration of action offers little, if any, advantage in this setting.

Therefore, it is important to choose that combination of agents that will promote hemodynamic stability in a particular patient with his or her unique hemodynamic presentation. In this patient, I would use pancuronium in conjunction with the high-dose narcotic anesthetic.

Fleming N. Con: the choice of muscle relaxants is not important in cardiac surgery. *J Cardiothorac Vasc Anesth.* 1995;9:768–771.

Hudson RJ, Thomson IR. Pro: the choice of muscle relaxants is important in cardiac surgery. *J Cardiothorac Vasc Anesth.* 1995;9:768–771.

Thys DM, Hillel Z, Schwartz AJ, eds. *Textbook of Cardiothoracic Anesthesiology*. New York: McGraw-Hill; 2001:589–629.

C.8. What are the usual TEE findings in a patient with aortic stenosis, aortic insufficiency, or mitral regurgitation? How do you grade the severity of aortic stenosis by TEE? How do you quantify the severity of mitral regurgitation? What is the impact of aortic stenosis on the severity of mitral regurgitation?

The severity of aortic stenosis is usually stated in terms of aortic valve area. Normal aortic valve area is 2.5 to 3.5 cm^2. Moderate stenosis is when the aortic valve area is within the range of 0.8 to 1.2 cm^2 and severe stenosis when the aortic valve area is less than 0.8 cm^2. A patient with a large peak pressure gradient (usually more than 75 mm Hg) in the absence of excessively high cardiac output is usually considered to have severe aortic stenosis as well. In the setting of low cardiac outputs, the pressure gradient may not be that great (20 to 30 mm Hg), and determination of aortic valve area is required. This can be accomplished with echocardiography.

Mitral regurgitation is graded by the amount of blood regurgitated backward into the left atrium during systole. Doppler color flow permits quantification of this flow. Common methods for mitral regurgitation quantification include the depth of mitral regurgitation jet extent into the left atrium (25% mild mitral regurgitation, 25% to 75% moderate mitral regurgitation, and more than 75% severe mitral regurgitation). Other methods of quantification include calculation of the area of the regurgitant jet by planimetry, by comparison of the mitral regurgitation jet area to the area of the left atrium, and by analysis of pulmonary vein flow profiles. It is important to remember that the amount of regurgitant blood flow in the setting of mitral regurgitation is determined by the amount of time spent in systole, the size of the defect in the mitral valve, and the pressure gradient across the defect. Therefore, mitral regurgitation severity by Doppler color flow is load dependent. The lower pressure of the anesthetic state can often mask more severe degrees of mitral regurgitation seen when the patient is under his or her usual hemodynamic conditions.

The left ventricular pressures are increased in the setting of aortic stenosis. Therefore, the gradient across the mitral valve is increased often leading to more severe mitral regurgitation. Following replacement of the stenotic aortic valve and elimination of the outflow tract obstruction, left ventricular pressures are markedly reduced. Moderate levels of mitral regurgitation without major structural defects in the mitral valve apparatus usually revert to minimal or certainly less severe levels following reduction in the left ventricular outflow obstruction.

Carabello BA, Crawford FA Jr. Valvular heart disease. *N Engl J Med.* 1997;337:32–41.

Spain MG, Smith MD, Grayburn PA, et al. Quantitative assessment of mitral regurgitation by Doppler color flow imaging: angiographic and hemodynamic correlations. *J Am Coll Cardiol.* 1989;13:585–590.

C.9. What special considerations particular to cardiopulmonary bypass (CPB) operations do you have for each of the four lesions? Focus on these concerns with respect to the induction and prebypass, bypass, and postbypass periods.

Aortic Stenosis

Critical to the management of a patient with aortic stenosis is the avoidance of hypotension. Low blood pressure can initiate a cascade of events leading to cardiac arrest. Hypotension decreases the gradient for coronary perfusion with resultant ischemia. Ischemia leads to diminished cardiac output and decreased blood pressure further compromising coronary perfusion. The occurrence of cardiac arrest in a patient with aortic stenosis is particularly catastrophic because closed-chest cardiac massage will provide little gradient for blood flow across a stenotic aortic valve.

Patients with aortic stenosis are particularly dependent on their atrial kick for adequate ventricular filling volume and can rapidly become hypotensive and ischemic following the onset of supraventricular tachycardia or atrial fibrillation. These rhythms are not uncommon during atrial cannulation. Therefore, it is of particular importance that every preparation for the initiation of CPB be made before atrial manipulation. Increased muscle mass of ventricular hypertrophy can be more difficult to adequately protect with cardioplegia. Careful attention to surface cooling, myocardial temperature measurement, and the use of retrograde cardioplegia can be helpful. Following aortic valve replacement, hypertension from left ventricular output now unopposed by any valvular lesion can result in stress on suture lines and excessive bleeding. It is important to remember that the compliance of the left ventricle is unchanged by surgery and still critically dependent on adequate preload and sinus rhythm.

Aortic Insufficiency

Patients undergoing aortic valve replacement for aortic insufficiency can often present difficult management decisions. The usual treatment measures for hypotension (α-agonist) may have deleterious effects by increasing regurgitant volume. The use of combined α- and β-agonists (ephedrine, epinephrine, or infusions of dopamine or dobutamine) may be required. Although it would serve to lessen regurgitant volume, afterload reduction is beneficial in only a subset of patients with aortic insufficiency. Those patients with elevated LVEDP, reduced ejection fraction, diminished cardiac output, and systemic hypertension usually benefit from afterload reduction. In contrast, those patients without the previously mentioned constellation may experience a decrease in forward cardiac output secondary to diminished preload from reduced venous return. Systemic hypotension usually limits the utility in the acute setting. The presence of aortic insufficiency makes initiation of CPB a critical period. Periods of bradycardia or ventricular fibrillation can lead to rapid volume overload of the left ventricle through the incompetent aortic valve. Pacing, electrical defibrillation, and/or cross-clamping should be performed to prevent ventricular distention. Similarly, myocardial protection is compromised by aortic insufficiency. Generation of adequate root pressures is usually not obtainable; hence, delivery of cardioplegia requires aortotomy and cannulation of the coronary ostia. Use of retrograde cardioplegia is advantageous. Following aortic valve replacement, the ventricle no longer has the lower pressure/impedance outflow afforded by the low aortic diastolic pressure. Inotropic support is often required. As

with aortic stenosis, the presence of an aortic suture line necessitates rapid response to hypertension to avoid bleeding and dissection.

Mitral Stenosis

Patients undergoing mitral valve replacement for mitral stenosis are particularly challenging. Marked elevations in pulmonary vascular resistance can be present with associated right heart failure. Stasis in the left atrium necessitates careful echocardiographic examination for the presence of atrial thrombi. Manipulation of the heart before cross-clamping should be avoided. Following replacement, the chronically underfilled, underworked left ventricle may be unable to handle the new volume load. Inotropic support is often required for right ventricular failure and occasionally to improve left ventricular function. Afterload reduction and improved systemic perfusion through an IABP may be beneficial.

Mitral Regurgitation

Similarly, patients with mitral regurgitation may have pulmonary hypertension and right heart failure. In contrast to aortic insufficiency, almost all patients with mitral regurgitation can be greatly benefited by afterload reduction, both pharmacologically and through an IABP. Diminution of left ventricular systolic pressure through afterload reduction decreases the pressure gradient from the left ventricle to the left atrium during systole, with resultant decreased regurgitant volume.

Prebypass assessment can be misleading. Preserved ejection fractions and elevated stroke volumes may mask marked left ventricular systolic dysfunction. It should be remembered that much of the left ventricular volume is ejected into the low-pressure/impedance outflow path of the left atrium. This route is no longer available after valve replacement. Following mitral valve replacement, dysfunctional ventricles may be unable to provide adequate forward flow into the systemic circuit with its elevated vascular resistance and usually necessitate the use of inotropic support.

Patients previously in atrial fibrillation without marked atrial enlargement often revert to or can be converted to sinus rhythm following valve replacement. The capacity of maintaining a person in sinus rhythm dramatically decreases when the diameter of the atrium is more than 5 cm.

Hartman GS. *Management of Patients with Valvular Heart Disease*. Cleveland: International Anesthesia Research Society; 1994:141–151. 1994 IARS Review Course Lectures.

Kaplan JA, Reich DL, Konstadt SN, eds. *Cardiac Anesthesia*. 4th ed. Philadelphia: WB Saunders; 1999:727–784.

Thys DM, Hillel Z, Schwartz AJ, eds. *Textbook of Cardiothoracic Anesthesiology*. New York: McGraw-Hill; 2001:589–629.

C.10. The patient cannot be weaned from CPB following an aortic valve replacement and mitral valve replacement. What are the possible causes?

The adequacy of myocardial preservation should be considered. LVH without or with accompanying coronary artery disease increases myocardial oxygen demands. Prolonged cross-clamp time necessitated by dual valve replacement can lead to inadequate and/or nonhomogeneous myocardial protection. In addition, there may be residual cardioplegia present within the myocardium. Therefore, some degree of postbypass left ventricular dysfunction can be anticipated. Inotropic support may be required. It is important to remember that although the obstruction to left ventricular ejection is acutely relieved by replacement of the stenotic valve, left ventricular compliance is largely unchanged. Adequate preload still depends on sinus rhythm and sufficient left ventricular filling pressures (pulmonary artery occlusion pressure [PAOP] or LVEDP).

Elevations in pulmonary vascular resistance may render estimation of left atrial pressure through the pulmonary artery catheter inaccurate. In this setting, placement of an left atrial catheter is indicated. TEE may prove invaluable in identifying surgically correctable causes for inability to wean from CPB. Evaluation of left ventricular filling and contractility can help resolve the situation of low cardiac output and high filling pressures. A small underfilled left ventricle with hyperdynamic contractility and a dilated, overfilled, hypokinetic left ventricle can both give the same hemodynamic parameters but obviously require different pharmacologic interventions. Abnormal valve seating may compromise flow into the coronary ostia and return to bypass with valve repositioning or coronary artery bypass grafting may be indicated. Similarly, perivalvular leaks or aortic dissections can be readily identified. Iatrogenic injury to the circumflex artery, although rare, can occur during mitral valve annuloplasty or replacement. The course of the circumflex artery along the posterior path of the mitral valve annulus makes it a potential target for errant valve stitches. New regional wall motion abnormalities in the inferior-lateral territory may help to make this unusual diagnosis or influence the decision to pursue diagnostic testing, such as emergent cardiac catheterization. The coronary sinus can also be damaged during mitral valve repair and replacement as the suture line is placed in the lateral mitral annulus. TEE may demonstrate abnormal echodensities in the area of the atrioventricular groove, and color flow Doppler can demonstrate high-velocity flow jets from the chambers to the sinus.

Ender J, Selbach M, Borger MA, et al. Echocardiographic Identification of Iatrogenic Injury of the Circumflex Artery During Minimally Invasive Mitral Valve Repair. *Ann Thorac Surg*. 2010;89:1866–1872.

Thomas SJ, Kramer JL, eds. *Manual of Cardiac Anesthesia*. 2nd ed. New York: Churchill Livingstone; 1993:81–127.

Thys DM, Hillel Z, Schwartz AJ, eds. *Textbook of Cardiothoracic Anesthesiology*. New York: McGraw-Hill; 2001:589–629.

C.11. How would you diagnose right heart failure and pulmonary hypertension? How would you treat it?

Right heart failure is diagnosed by the elevations in right-sided filling pressures, specifically central venous pressure. Careful examination is required to rule out tricuspid insufficiency as the cause of the central venous pressure elevation. A high central venous pressure indicates the inability of the right heart to adequately propel the venous return volume into the pulmonary circulation. Elevation in pulmonary artery pressures is indicative of pulmonary hypertension. The combination of high central venous pressure and high pulmonary artery pressures indicates severe right heart failure. This scenario can be difficult to manage. Attempts to elevate systemic perfusion pressure with α-agonists can worsen pulmonary hypertension. Administration of vasodilators to lower pulmonary pressures results in systemic hypotension. In this setting, it is often prudent to return to CPB, relieve ventricular distention, and improve myocardial perfusion. During this "rest period," adjustments in inotropic therapy, ventilation, and cardiac rhythm can be instituted. Optimization of acid–base status and hemoglobin concentration should also be performed. Separation from bypass can then be reattempted.

Typical inotropic agents effective in this setting are those with high degrees of β-adrenergic potency and potent vasodilation in the pulmonary vasculature. Commonly employed agents include dobutamine, epinephrine, prostaglandin E_1 and the phosphodiesterase-III (PDE-III) inhibitors amrinone and milrinone. It is not uncommon to require the administration of α-agonists to counteract the systemic vasodilating effects of prostaglandin E_1 and the PDE-III agents. Some selective pulmonary vasodilating action and systemic vasoconstricting effects can often be achieved by administration of pulmonary vasodilating agents such as prostaglandin E_1 through the right-sided access (central venous pressure or pulmonary artery catheter) and

infusion of the α-agonists through the left arterial line, thereby minimizing vasoconstriction of the pulmonary arterial bed.

Nitric oxide is a potent, inhaled pulmonary vasodilator. Its half-life in the systemic circulation is extremely short, permitting its administration to the pulmonary vasculature with minimal systemic hypotensive effects. Nitric oxide can selectively and effectively dilate the pulmonary vasculature. The exact method of delivery, scavenging of waste gases, and high cost remain as obstacles to its clinical application.

Body SC, Hartigan PM, Shernan SK, et al. Nitric oxide: delivery, measurement, and clinical application. *J Cardiothorac Vasc Anesth.* 1995;9:748–763.

Kieler-Jensen N, Houltz E, Ricksten SE. A comparison of prostacyclin and sodium nitroprusside for the treatment of heart failure after cardiac surgery. *J Cardiothorac Vasc Anesth.* 1995;9:641–646.

Savage RM, Aronson S, eds. Assessment of the right ventricle. In: *Comprehensive Textbook of Intraoperative Transesophageal Echocardiography*. Philadelphia: Lippincott Williams & Wilkins; 2005:147–155.

C.12. How does an intra-aortic balloon pump (IABP) work to benefit the failing heart?

An IABP is a catheter with a large balloon (40 to 60 mL) at its tip. It is positioned in the thoracic aorta distal to the left subclavian artery origin and proximal to the take-off of the renal vessels. It is timed to inflate during diastole to increase diastolic perfusion pressure to the coronary arteries, great vessels, and major abdominal organs and to deflate just before systole, creating a void in volume within the aorta and thus a low pressure with resultant decrease in afterload. The decreased afterload increases stroke volume and hence forward cardiac output. It is a unique modality that can improve coronary perfusion pressures while reducing myocardial oxygen demand.

Baskett RJ, Ghali WA, Maitland A, et al. The intraaortic balloon pump in cardiac surgery. *Ann Thorac Surg.* 2002;74:1276–1287.

Cheung AT, Savino JS, Weiss SJ. Beat-to-beat augmentation of left ventricular function by intraaortic counterpulsation. *Anesthesiology*. 1996;84:545–554.

C.13. What role does the IABP have in this setting?

An IABP may be useful because unlike any pharmacologic maneuver it is capable of increasing mean pressure during diastole critical for coronary perfusion while lowering afterload to systolic left ventricular ejection. Myocardial dysfunction secondary to inadequate protection during bypass can be reduced by decreased afterload and augmentation of diastolic pressures through IABP counterpulsation. Studies have shown superior survival among patients with isolated cardiac artery bypass graft (CABG) treated with IABP's compared with patients undergoing non-CABG cardiac surgeries. The IABP can only aid patients in whom ventricular function can recover in a relatively short time. Outside of this population, ventricular assist devices may be more appropriate.

Baskett RJF, Ghali WA, Maitland A, Hirsch G. The intraaortic balloon pump in cardiac surgery. *Ann Thorac Surg.* 2002;74:1276–1287.

Cheung AT, Savino JS, Weiss SJ. Beat-to-beat augmentation of left ventricular function by intraaortic counterpulsation. *Anesthesiology.* 1996;84:545–554.

C.14. What role does TEE play in the placement, timing, and demonstration of efficacy of an IABP?

The thoracic aorta and aortic arch can be clearly imaged by TEE. Imaging of the take-off of the left subclavian artery facilitates optimal positioning of the IABP. In addition, before insertion the aorta can be evaluated for dissection or the presence of severe atheromatous disease, both contraindications to IABP insertion. TEE can demonstrate the efficacy of an IABP by showing enhanced ventricular emptying during systole and filling during diastole.

C.15. How would you properly time the IABP cycle?

Inflation should occur just following the dicrotic notch and deflation before the upstroke in the aortic pressure curve. Augmentation in pressures during diastole and mean pressures should occur. Diastolic pressure (the lowest pressure in the cardiac cycle) should in fact fall. Peak pressure generated by the left ventricle or systolic pressure should fall while the balloon generated pressure during ventricular diastole (augmented pressure) should increase.

C.16. What are the contraindications to the use of an IABP?

The most common contraindications are severe aortic insufficiency and severe aortic disease, atheromatous, aneurysmal, or a dissection. Although often listed as absolute contraindications, there are reports of the effective use of IABP in these settings. TEE can be helpful in evaluating the effect of an IABP on overall ventricular function. End-systolic areas should decrease, and end-diastolic areas should at least not increase but may decrease as well.

Sanfelippo PM, Baker NH, Ewy HG, et al. Experience with intraaortic balloon counterpulsation. *Ann Thorac Surg.* 1986;41:36–41.

C.17. What is the role for ventricular assist devices?

Ventricular assist devices are used in the management of chronic heart failure after exhausting medical therapy. These devices can be used as a bridge to transplantation or as a destination therapy in those who do not qualify for transplantation. The short-term use of ventricular assist devices includes patients with refractory heart failure in the immediate postoperative setting. Historically, the operative mortality associated with postcardiotomy assist devices was very high. Newer machines utilize smaller cannulas and have smaller, more efficient pumps. The magnetically suspended centrifugal pumps are associated with minimal trauma to red blood cells or pump failures. The use of these devices is rapidly expanding, and early indications are improved mortality for patients experiencing postcardiotomy shock with recoverable myocardium. Ventricular assist devices are used for right, left, and biventricular support.

Bhama JK, Kormos RL, Toyoda Y, et al. Clinical experience using the Levitronix Centrimag System for temporary right ventricular mechanical circulatory support. *J Heart Lung Transpl.* 2009:971–976.

DeRobertis F, Birks EJ, Rogers P, et al. Clinical performance with the Levitronix Centrimag Short-tern Ventricular Assist Device. *J of Heart Lung Transpl.* 2006:181–186.

Noon GP, Lafuente JA, Irwin S. Acute and temporary ventricular support with BioMedicus Centrifugal Pump. *Ann Thorac Surg.* 1999;68:650–654.

D. Postoperative Management

D.1. In the intensive care unit (ICU) 4 hours later, the patient became hypotensive with a low cardiac output. How could you distinguish between cardiac tamponade and pump failure? How would the TEE images differ?

The differentiation between cardiac tamponade and primary pump failure in the immediate postbypass-ICU setting can be difficult. Elevations in filling pressures, systemic hypotension, and low cardiac output are consistent with both diagnoses. The classic teaching of equalization of cardiac pressures seen in a "fluid" tamponade may not be present because areas of focal compression from clot can markedly reduce filling of only one chamber in the absence of an intact pericardium. Echocardiography can be beneficial in this setting by permitting visualization of chamber volume and function. The transesophageal approach has particular advantage over TTE in the postoperative setting in which the usual transthoracic window may be obscured by dressings and drainage tubing. Focal compression of the cardiac chambers from a clot or pericardial effusion can readily be distinguished from a volume-overloaded, failing heart with poor myocardial contractility. When the diagnosis is not clear, however, surgical re-exploration may be indicated. (See Chapter 11, Cardiac Tamponade.)

Bommer WJ, Follette D, Pollock M, et al. Tamponade in patients undergoing cardiac surgery: a clinical-echocardiographic diagnosis. *Am Heart J*. 1995;130:1216–1223.

Flynn BC, Spellman J, Bodian C, Moitra V. Inadequate visualization and reporting of ventricular function from transthoracic echocardiography after cardiac surgery. *J Cardiothorac Vasc Anesth*. 2010;24:280–284.

Price S, Prout J, Jaggar SI, et al. 'Tamponade' following cardiac surgery terminology and echocardiography may both mislead. *Eur J Cardio Surg*. 2004:1156:1160.

D.2. Would you extubate this patient early in the ICU? Why?

No. This patient has undergone a double valve replacement. In this more complex procedure, coagulopathy and postoperative bleeding, hypothermia from incomplete and nonuniform rewarming, and pulmonary hypertension are not uncommon occurrences in the immediate postoperative period. Sedation, paralysis, and mechanical ventilation can reduce the oxygen requirements during this early phase of recovery, minimize pulmonary hypertension secondary to hypercarbia, and permit reestablishment of core temperatures.

Cheng DCH. Pro: early extubation after cardiac surgery decreases intensive care unit stay and cost. *J Cardiothorac Vasc Anesth*. 1995;9:460–464.

Guenther CR. Con: early extubation after cardiac surgery decreases intensive care unit stay and cost. *J Cardiothorac Vasc Anesth*. 1995;9:465–467.

D.3. What are the advantages and disadvantages of early extubation?

The advantages of early extubation are both medical and financial. Early extubation can lessen the adverse sequelae from prolonged endotracheal intubation, including epithelial damage, decreased ciliary motility, and diminished mobilization of secretions. Positive pressure ventilation can have adverse effects on venous return. Nevertheless, the overwhelming drive toward early extubation is cost and patient comfort. Early extubation can decrease cost by decreasing ICU staff requirements, decreasing the cost of sedatives, lessening the duration of ICU stays, and improving operating room use by lessening cancellation of cases secondary to blocked ICU beds.

The potential advantages of early extubation, both financial and physiologic, must be weighed against the potential disadvantages of early extubation. The potential for respiratory compromise leading to hypoxemia, hypercarbia, ischemia, and the potential for infarction and neurologic injury is real. Any savings realized from early extubation can be rapidly lost by one adverse event. Success relies on careful integration of all players in the care of the patient undergoing cardiac surgery, from the management of intraoperative anesthetic techniques to the organization of the ICU and staff and the provision of postoperative analgesia. Equally important to the success of an early extubation program is appropriate patient selection.

Cheng DCH. Pro: early extubation after cardiac surgery decreases intensive care unit stay and cost. *J Cardiothorac Vasc Anesth*. 1995;9:460–464.

Guenther CR. Con: early extubation after cardiac surgery decreases intensive care unit stay and cost. *J Cardiothorac Vasc Anesth*. 1995;9:465–467.

Kogan A, Ghosh P, Preisman S, et al. Risk factors for failed "fast-tracking" after cardiac surgery in patients older than 70 years. *J Cardiothorac Vasc Anesth*. 2008;22:530–535.

E. Alternative Treatments

E.1. What are the percutaneous options for mitral valve repair?

In 1991, Otavio Alfieri described a surgical correction of mitral regurgitation using a technique of suturing the middle portions of the two mitral leaflets together. The resultant double orifice valve is an adequate solution for many mitral valve lesions. Based on this principle, a percutaneous treatment for mitral regurgitation has emerged.

E.2. How is percutaneous mitral valve repair performed?

The MitraClip is a small, polyester fabric-covered cobalt-chromium clip that is applied to the mitral leaflets, to mimic the surgical procedure described above. The device is delivered percutaneously via a femoral venous, transseptal approach. Although this device is still in trials, the initial results are favorable to reduce mitral regurgitation to less than 2+. General anesthesia is typically used.

Feldman T, Kar S, Rinaldi M, et al. for the EVEREST Investigators. Percutaneous mitral repair with the MitraClip system. *JACC*. 2009;54:686–694.

Hussaini A, Kar S. Percutaneous mitral valve repair: potential in heart failure management. *Curr Heart Fail Rep*. 2010;7:22–26.

E.3. What are the percutaneous options for aortic valve repair and replacement?

Surgical valve replacement is the treatment of choice for severe aortic stenosis. For those patients at very high risk for surgery, alternative treatments may be preferable. Aortic balloon valvuloplasty has been a nonsurgical option since the 1980s. Although it is far less invasive than surgery, high complication rates and in-hospital mortality have reserved this treatment for a select population. In addition, high restenosis rates make this a short-lived solution. Percutaneous aortic valve replacement is emerging as another alternative to surgery in the high-risk population.

Billings FT, Kodali SK, Shanewise JS. Transcatheter aortic valve implantation: anesthetic considerations. *Anesth Analg*. 2009;108:1453–1462.

Hara H, Pedersen WR, Ladich E, et al. Percutaneous balloon aortic valvuloplasty revisited: time for a renaissance? *Circulation*. 2007;115:e34–e338.

E.4. How is percutaneous aortic valve replacement performed?

Currently, two devices are in human trials. The percutaneous devices are bioprosthetic valves mounted in self-expanding nitinol stents. The valves may be delivered by femoral artery retrograde or transapical antegrade approaches. After balloon valvuloplasty, the valve-stent is deployed. Rapid ventricular pacing is used to decrease cardiac translation and minimize ejection pressure during deployment. Transesophageal and fluoroscopic guidance are used. Complications of these procedures include iliac artery avulsion, aortic dissection, atherosclerotic embolic events, and renal injury secondary to radiocontrast exposure.

E.5. What anesthetic techniques and monitors are used?

General anesthesia is mostly used to allow for simultaneous TEE examination and in the case of thoracotomy for the transapical approach. Large-bore central venous access is necessary in the event of vascular injury or to administer vasoactive medications. Pulmonary artery catheters are frequently used in percutaneous atrial valve replacement procedures. Alternatively, local infiltration and intravenous sedation may be used for these procedures. In these cases, TTE examination is performed for evaluation at the conclusion of the procedure. Radial artery catheters are placed before induction for continuous monitoring and for arterial blood gases analysis.

Billings FT, Kodali SK, Shanewise JS. Transcatheter aortic valve implantation: anesthetic considerations. *Anesth Analg*. 2009;108:1453–1462.

Covello RD, Maj G, Landoni G, et al. Anesthetic management of percutaneous aortic valve implantation: focus on challenges encountered and proposed solutions. *J Cardiothorac Vasc Anesth*. 2009;23:280–285.

E.6. What is minimally invasive cardiac valve surgery?

The Society of Thoracic Surgeons database considers "any procedure not performed with a full sternotomy and cardiopulmonary bypass support" a minimally invasive procedure. The practical applications of "mini-valve surgery" include partial sternotomy, thoracotomy, and video-assisted and robot-assisted procedures. The downside to minimally invasive approaches include difficulty converting to a sternotomy in the case of cannula displacement or aortic dissection and complications of femoral artery cannulation (including arterial dissection, infection, and hematoma). The anesthetic management varies from standard sternotomy cases, including single-lung ventilation for thoracotomy approaches and transjugular coronary sinus catheters, to provide retrograde cardioplegia. Intraoperative TEE is especially critical in these cases to monitor for cardiac distention, removal of air, and cannula placement. There is clearly a significant learning curve to provide an equivalent surgical outcome with a "mini" versus traditional strategy. In successful procedures, patients enjoy improved cosmesis and decreased bleeding, wound infection, pain, and hospital length of stay. Unfortunately, in high-risk patients, the increased time of aortic cross-clamping and CPB may be deleterious. Also, complications are extremely morbid, including aortic dissection and death. Mini-valve surgery is limited to patients with an isolated valve disease.

Schmitto JD, Mokashi SA, Cohn LH. Minimally-invasive valve surgery. *JACC*. 2010;56:455–462.

CHAPTER 7

Pacemakers, Implantable Cardioverter-Defibrillators, and Cardiac Resynchronization Therapy Devices

Alan Cheng and Fun-Sun F. Yao

A 63-YEAR-OLD WOMAN

was scheduled for urgent open cholecystectomy. She underwent a dual-chamber permanent pacemaker (PPM) implantation 10 years ago for sick sinus syndrome and intermittent heart block. The pacemaker was upgraded to an implantable cardioverter-defibrillator (ICD) with cardiac resynchronization therapy (CRT) 9 months ago because of ischemic cardiomyopathy and worsening heart failure symptoms in the setting of a left bundle branch block. Her blood pressure was 110/68 mm Hg, and her heart rate was regular at 60 beats per minute. An electrocardiogram (ECG) obtained on admission demonstrated atrioventricular (AV) sequential pacing.

A. Medical Disease and Differential Diagnosis

1. What are the indications for PPMs?
2. What is sick sinus syndrome?
3. How would you diagnose first-, second-, and third-degree AV block, right bundle branch block (RBBB) with left anterior fascicular hemiblock, and left posterior fascicular hemiblock?
4. Is it necessary to insert a temporary pacemaker before general anesthesia for an asymptomatic patient with bifascicular or trifascicular block?
5. What are the three-letter and five-letter identification codes of the North American Society of Pacing and Electrophysiology (NASPE) and British Pacing and Electrophysiology Group (BPEG) generic (NBG) code for pacemaker classification?
6. How many modes of pacing are available in modern-day PPMs? How do they work? What is the difference between DDD pacing and DDI pacing?
7. The patient was mechanically hyperventilated during surgery and her pacemaker gradually increased her heart rate. What feature of the PPM is accounting for this?

8. What are the advantages and disadvantages of atrial pacing only? What are the disadvantages of ventricular pacing?
9. What are the indications for and complications associated with AV sequential PPMs?
10. How would you know if the patient's PPM was atrially, ventricularly, or atrioventricularly sequentially pacing?
11. What is the maximum amount of energy that a modern PPM can provide in terms of pulse amplitude and pulse width?
12. During a PPM implantation, what are the acceptable values for modern pacemaker leads in terms of pacing thresholds, amplitude of sensed intrinsic activity and impedance?
13. What is a biventricular PPM or CRT device? What are the indications for such a device?
14. What are the usual life spans of PPMs and ICDs?
15. What is an ICD? How does it work?
16. What are the indications for ICDs?
17. What is the NASPE and BPEG generic defibrillator (NBD) code?

B. Preoperative Evaluation and Preparation

1. How would you preoperatively evaluate the patient described earlier?
2. How do you determine whether the patient has a cardiac implantable electronic device (CIED) and define what type of CIED?
3. How do you determine whether the patient is dependent on the pacing function of the CIED?
4. How do you know if the implanted PPM or ICD is working?
5. What information would you like to obtain from interrogating this device?
6. How do you preoperatively prepare the patient for surgery and anesthesia?
7. Would you recommend reprogramming this device to asynchronously pace before surgery? What would you recommend regarding the ICD functions of the device?

C. Intraoperative Management

1. How would you monitor this patient?
2. What drugs and equipment would you like to have on hand in the operating room?
3. How would you set up the transcutaneous external pacer and defibrillator?
4. Had this patient's ICD been implanted the day before surgery, would you consider avoiding certain inhalational gases for anesthesia?
5. Electromagnetic interference (EMI) from electrocautery during the case results in significant noise on your cardiac monitor. You recall that EMI can also inhibit pacing function from the pacemaker. In this pacemaker-dependent patient, how can you determine whether inappropriate inhibition of the pacemaker is occurring?
6. What are the potential responses of pacemakers and ICDs to electrocautery?
7. How would you prevent the effects of EMI on the pacemaker or ICD from the electrocautery?
8. What are the effects of a magnet over pacemakers and ICDs?
9. In the middle of surgery, the patient developed ventricular tachycardia. What would you do?
10. What precautions should be taken when a patient with a CIED is undergoing extracorporeal shock wave lithotripsy (ESWL)?

11. Is electroconvulsive therapy (ECT) contraindicated in patients with pacemakers or ICDs?
12. Is magnetic resonance imaging (MRI) contraindicated in patients with a CIED?
13. What are the precautions during radiofrequency ablation for a patient with a CIED?

D. Postoperative Management

1. How would you monitor this patient in the postanesthesia care unit?
2. How would you confirm that the CIED is functioning properly after surgery?

A. Medical Disease and Differential Diagnosis

A.1. What are the indications for PPMs?

Artificial pacing is generally indicated for the treatment of symptomatic bradycardia of any origin. The two major indications for permanent pacing are failure of impulse formation and failure of cardiac conduction. Clinically, sick sinus syndrome and complete heart block are the most common indications for pacemakers. The following conditions are class I and IIA indications for a PPM:

- Sinus node dysfunction with documented symptomatic bradycardia, chronotropic incompetence, or symptomatic sinus bradycardia secondary to required drug therapy for medical conditions
- Sinus node dysfunction for heart rates less than 40 beats per minute when a clear association between symptoms consistent with bradycardia and the actual presence of bradycardia is absent
- Recurrent syncope caused by spontaneous carotid sinus hypersensitivity or greater than 3-second episode of ventricular asystole induced with carotid sinus pressure
- Third-degree or advanced second-degree AV block associated with bradycardia with symptoms or ventricular arrhythmias presumed secondary to AV block
- Asymptomatic third-degree or advanced second-degree AV block in patients with sinus rhythm and documented periods of asystole greater than 3 seconds, escape rate less than 40 beats per minute, or an escape rhythm that is below the AV node (as suggested by a wide QRS complex)
- Ventricular pauses of greater than 5 seconds in patients with atrial fibrillation with bradycardia
- Third-degree or advanced second-degree AV block resulting from catheter ablation or cardiac surgery
- First- or second-degree AV block associated with symptoms similar to those of pacemaker syndrome or hemodynamic compromise
- Chronic bifascicular block with advanced second-degree AV block or intermittent third-degree AV block
- Chronic bifascicular block with alternating left bundle branch block (LBBB) and RBBB conduction
- High-risk patients with congenital long QT syndrome or those with documented sustained pause-dependent ventricular tachycardia
- New York Heart Association class III or class IV heart failure symptoms despite optimal medical therapy in patients with dilated cardiomyopathy (ejection fraction less than 35%), QRS duration greater than 120 milliseconds and sinus rhythm (e.g., biventricular pacing)

Atlee JL, Bernstein AD. Cardiac rhythm management devices (part I). *Anesthesiology.* 2001;95:1265–1280.

Epstein AE, DiMarco JP, Ellenbogen KA, et al. ACC/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2008;117:e350–e408.

Libby P, Bonow RO, Mann DL, et al., eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 8th ed. Philadelphia: Saunders; 2008:831–835.

Salukhe TV, Dob D. Pacemakers and defibrillators: anesthetic implications. *Br J Anesth*. 2004;93:95–104.

A.2. What is sick sinus syndrome?

Sick sinus syndrome describes an array of clinical disorders resulting from irreversible sinus node dysfunction. This may be manifested by episodes of sinus arrest, sinus pause, or bradycardia secondary to inadequate sinus node automaticity. As a result, episodes of tachyarrhythmias from ectopic atrial foci can occur as well. Extended cardiac telemetry such as 24-hour Holter monitoring is helpful to make a diagnosis. When episodes of tachycardia and bradycardia coexist, it is often referred to as *tachy-brady* syndrome. This is one of the most common indications for pacemakers and is characterized by the following:

- Unexpected persistent severe sinus bradycardia
- Episodes of sinus arrest or exit block
- Paroxysmal or chronic atrial fibrillation or atrial flutter
- Alteration of paroxysms of rapid regular or irregular atrial tachyarrhythmias and periods of slow atrial and ventricular rates (tachy-brady syndrome)
- Slow return to sinus rhythm following cardioversion
- Lack of increase in sinus rate above 90 beats per minute following intravenous administration of 1.5 to 2 mg atropine

Dobrzynski H, Boyett MR, Anderson RH. New insights into pacemaker activity: promoting understanding of sick sinus syndrome. *Circulation*. 2007;115:1921–1932.

Libby P, Bonow RO, Mann DL, et al., eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 8th ed. Philadelphia: Saunders; 2008:909–913.

Mangrum JM, DiMarco JP. The evaluation and management of bradycardia. *N Engl J Med*. 2000;342:703–709.

A.3. How would you diagnose first-, second-, and third-degree AV block, right bundle branch block (RBBB) with left anterior fascicular hemiblock, and left posterior fascicular hemiblock?

First-degree AV block is characterized by a PR interval of greater than 0.20 seconds during normal sinus rhythm (Fig. 7.1). Second-degree AV block is subdivided into two types. Mobitz type I, or Wenckebach block, is characterized by a progressively lengthening PR interval, which occurs until a P wave is not conducted down the AV node and a QRS complex is dropped. The site of block is typically in the AV node. Mobitz type II block is characterized by a loss of AV conduction with no progressive lengthening of the PR interval before the sudden dropping of one or more QRS complexes. The site of block is typically below the AV node and within the His-Purkinje system. Third-degree AV block, also called complete heart block, occurs when all electrical activity from the atrium fails to progress into the Purkinje system. The site of block can lie in either the AV node or the His-Purkinje system. The atrial and ventricular contractions have no relation with each other. As a result, the QRS complexes seen result from an ectopic focus either from the ventricular myocardium or in an area of



First-degree heart block. Sustained prolongation of the PR interval with no dropped QRS complexes.



Second-degree heart block, type I. Also referred to as Wenckebach block or Mobitz I, there is progressive prolongation of the PR interval before the dropped QRS complex. The PR interval of the first return QRS complex has normalized compared to the PR interval of the QRS complex of the last beat before dropping. This behavior suggests that the location of block occurs in the AV node.



Second-degree heart block, type II. Also referred to as Mobitz II, there is no progressive increase in the PR interval before the dropped QRS complex. This suggests that the location of the block occurs below the AV node. Note also the QRS morphology during conducted beats. The wide QRS complex suggests the presence of infranodal disease, which is often seen in the presence of Mobitz II heart block.



Third-degree heart block. The P waves mark through with no communication with the ventricular beats.

Figure 7.1 Atrioventricular heart block.

the AV node/His-Purkinje system below the site of block. Therefore, the QRS complex may appear wide or narrow, respectively, and typically occur with a rate of 40 to 60 beats per minute.

RBBB with left anterior hemiblock is present when the ECG shows an RBBB with a left axis deviation (usually greater than −60 degrees) in the absence of an inferior myocardial infarction. Complete RBBB with right axis deviation (greater than

90 degrees) is indicative of RBBB and left posterior hemiblock in the absence of a lateral myocardial infarction or evidence of right-sided heart failure.

Libby P, Bonow RO, Mann DL, et al., eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 8th ed. Philadelphia: Saunders; 2008:167–172, 913–921.

A.4. Is it necessary to insert a temporary pacemaker before general anesthesia for an asymptomatic patient with bifascicular or trifascicular block?

The risk for progression to complete heart block in asymptomatic patients with bifascicular block is low. Further, no clinical characteristics have been identified that accurately predict the risk of development of complete heart block. Therefore, routine pacemaker (PPM) implantation in patients with asymptomatic bifascicular block is not recommended. Observations made in the perioperative period have suggested that development of complete heart block during general anesthesia is also rare; therefore, it is generally not recommended that patients undergo temporary pacemaker insertion before general anesthesia. However, it is advisable to have an external pacemaker available in the operating room. Trifascicular heart block describes patients with a bifascicular block and prolongation of the PR interval. This term is somewhat of a misnomer because, in truth, if all three fascicles (i.e., right bundle, left anterior bundle, left posterior bundle) were blocked, the patient would be in complete heart block. Although it is generally agreed that individuals with trifascicular block have a higher risk for sudden death, there is no single clinical variable that predicts a higher risk for complete heart block during surgery. Small case series have shown that the development of intraoperative complete heart block in asymptomatic patients with trifascicular block is uncommon. Therefore, routine temporary pacemaker insertion before general anesthesia in these patients is not recommended.

Berg GR, Kotler MN. The significance of bilateral bundle branch block in the preoperative patient. *Chest*. 1971;59:62–67.

Gauss A, Hubner C, Radermaker P, et al. Perioperative risk of bradyarrhythmias with asymptomatic chronic bifascicular block or left bundle block: does an additional first degree atrioventricular block make any difference? *Anesthesiology*. 1998;88:679–687.

Libby P, Bonow RO, Mann DL, et al., eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 8th ed. Philadelphia: Saunders; 2008:832.

Trohman RG, Kim MH, Pinski SL. Cardiac pacing: the state of the art. *Lancet*. 2004;364:1701–1719.

A.5. What are the three-letter and five-letter identification codes of the North American Society of Pacing and Electrophysiology (NASPE) and British Pacing and Electrophysiology Group (BPEG) generic (NBG) code for pacemaker classification?

Given the complexity of current pacemaker systems, the Intersociety Commission for Heart Disease Resources established a classification code in the 1970s that is now widely accepted. The original nomenclature involved a three-letter identification code, as shown in the first three columns of Table 7.1. In 1980, this code was extended to five letters; the last two letters can be deleted when not applicable. In 1987, this five-letter coding system become known as the NBG pacemaker code after being adopted by both the NASPE (now known as the *Heart Rhythm Society*) and BPEG. The first letter describes the chamber(s) that the pacemaker can pace, the second letter describes the chamber(s) that it senses, and the third letter describes the response

Table 7.1 NASPE/BPEG Generic (NBG) Pacemaker Identification Code[a]

LETTER I CHAMBER(S) PACED	LETTER II CHAMBER(S) SENSED	LETTER III MODE OF RESPONSE	LETTER IV PROGRAMMABILITY RATE MODULATION	LETTER V ANTITACHYARRHYTHMIA FUNCTION(S)
O = None	O = None	O = None	O = None	O = None
A = Atrium	A = Atrium	T = Triggered	P = Single programmable	P = Pacing
V = Ventricle	V = Ventricle	I = Inhibited	M = Multiprogrammable	S = Shock
D = Dual (A + V)	D = Dual (A + V)	D = Dual (T + I)	C = Communicating	D = Dual (P + S)
			R = Rate modulation	

[a]Although the pacemaker identification coding involved the use of five letters, few modern pacemakers have antitachyarrhythmia functions. Therefore, most pacemakers are currently described by the first four letters of the coding system.
BPEG, British Pacing and Electrophysiology Group; NASPE, North American Society of Pacing and Electrophysiology; NBG, NASPE and BPEG Generic.

of the pacemaker to sensed intrinsic activity. The last two letters describe additional features such as rate responsiveness that are commonly omitted when not used. For example, a VVI pacing mode paces in the ventricle, can sense intrinsic activity in the ventricle, and inhibits pacing when it senses intrinsic activity. A VOO pacing mode paces in the ventricle but does not sense intrinsic activity; nor does it inhibit pacing—it simply paces regardless of the heart's electrical activity.

Libby P, Bonow RO, Mann DL, et al., eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 8th ed. Philadelphia: Saunders; 2008:831–832.

Practice advisory for the perioperative management of patients with cardiac implantable electronic devices: pacemakers and implantable cardioverter-defibrillators. An updated report by the American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Cardiac Implantable Electronic Devices. *Anesthesiology*. 2011;114:247–261.

A.6. How many modes of pacing are available in modern PPMs? How do they work? What is the difference between DDD pacing and DDI pacing?

Modern pacemakers are programmable into one of three modes of pacing: asynchronous pacing, single-chamber demand pacing, and dual-chamber AV sequential demand pacing. Asynchronous or fixed-rate (e.g., AOO, VOO, DOO [see section A.5 for details]) modes pace at a programmable preset rate that is independent of the inherent heart rate. They can be atrial, ventricular, or dual chamber. Competition and rarely induction of ventricular arrhythmias are the potential complications when pacing occurs in the presence of intrinsic myocardial electrical activity. Ventricular tachyarrhythmias can theoretically occur because the pacing spike can potentially be delivered during the vulnerable period of ventricular repolarization, resulting in an R on T phenomenon, but this is extremely rare.

Single-chamber demand pacing (e.g., AAI, VVI) paces at a preset rate only when the spontaneous heart rate drops below the programmed preset rate. For example, if this patient's device was programmed to VVI 70, the device would pace in the ventricle only when the native ventricular rate fell below 70 beats per minute. Once the native ventricular rate resumed above 70 beats per minute, the device would sense this activity and inhibit further pacing. Single-chamber demand pacing in the atrium functions in a similar way but is rarely used alone in the United States.

Dual-chamber AV sequential pacing requires two pacemaker leads, one in the right atrium and one in the right ventricle. The atrium is stimulated to contract first; then, after an adjustable PR interval (also referred to as the AV interval), the ventricle is stimulated to contract if no intrinsic ventricular activity is sensed by the ventricular pacing lead. For example, if this patient's device was programmed to DDD 70 with an AV interval of 200 milliseconds, the device would begin pacing the atrium first if the intrinsic sinus rate fell below 70 beats per minute. After the atrium has been paced, the device will wait for 200 milliseconds to sense intrinsic ventricular activity. If it does not see intrinsic activity within 200 milliseconds, it will then pace in the ventricle as well. DDD pacemakers can also pace in the ventricle in response to intrinsic atrial activity. For example, if the intrinsic atrial rate was 80 beats per minute, the device would inhibit pacing in the atrium because the base rate was set to 70 beats per minute. But because it is a dual-chamber device programmed to inhibit and trigger pacing in both chambers (i.e., the third "D" in the coding sequence), it will wait 200 milliseconds from the time of the intrinsic atrial activity and watch for intrinsic ventricular activity as well. If it sees intrinsic ventricular activity (i.e., the atrial signal conducted down the AV node and to the ventricle), it will inhibit ventricular pacing. If it does not see intrinsic ventricular activity occurring within 200 milliseconds from the intrinsic atrial activity, the pacemaker will then "trigger" the ventricular pacing lead to pace the ventricle. Dual-chamber pacemakers programmed to DDI differ slightly from devices programmed to DDD. In many ways, DDI programming is analogous to having a pacemaker with both AAI and VVI programming mode occurring simultaneously. AV sequential pacing occurs only when atrial pacing is present. This is in contrast to DDD pacing in which AV sequential pacing is preserved regardless of whether atrial pacing or atrial sensing is occurring. Similar to DDD programming, if the sinus rate fell below 70 beats per minute (as in this example), the atrial pacing lead would pace the atrium. After a 200-millisecond interval, if intrinsic ventricular activity was seen by the ventricular lead, then the ventricular lead would be inhibited from pacing the ventricle. If ventricular activity was not seen after 200 milliseconds, the ventricular lead would pace the ventricle. In contrast to DDD programming, if the sinus rate was above the preset rate and no atrial pacing was occurring, ventricular pacing would not be "triggered" after 200 milliseconds by these atrial sensed events and only occur if the *ventricular* rate fell below the preset rate of 70.

Libby P, Bonow RO, Mann DL, et al., eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 8th ed. Philadelphia: Saunders; 2008:837–840.

A.7. The patient was mechanically hyperventilated during surgery and her pacemaker gradually increased her heart rate. What feature of the PPM is accounting for this?

All modern pacemakers have the ability to adjust the pacing rate according to the patient's level of activity in an effort to obtain a more physiologic response to exercise. This is known as *rate-response* (adaptive) pacing and is denoted by an "R" in the fourth position of the NBG coding schema. Various activity-detecting systems have been developed to create a reliable rate-responsive pacemaker. They included muscle movement, respiratory rate, minute ventilation, central venous temperature, QT interval, myocardial contractility (dp/dt), oxygen saturation and pH in mixed venous blood, and ventricular depolarization gradient. Currently, PPMs used in the United States rely on sensors of motion or changes in minute ventilation. Because of the latter phenomenon, patients undergoing general anesthesia who are subjected to mechanical hyperventilation (e.g., neurosurgery) can experience an increase in the rate of pacing. Although it is generally not required to disable rate-responsive features before surgery, pacemaker-induced changes in heart rate resulting from intraoperative hyperventilation or significant motion may sometimes be mistaken for inadequate anesthesia. Hence, it is important that the anesthesia team be aware of the programmed settings

of the pacemaker. If reprogramming the device to disable rate-responsive features is not readily available, a magnet may be placed over the pacemaker site to temporarily convert it to asynchronous pacing. Although the response to a magnet may be programmed off in some pacemakers, all properly functioning pacemakers within the United States have magnet-responsive features activated as a default.

Ellenbogen KA, Kay GN, Lau CP, et al., eds. *Clinical Cardiac Pacing, Defibrillation and Resynchronization Therapy*. 3rd ed. Philadelphia: Elsevier; 2007:201–233.

A.8. What are the advantages and disadvantages of atrial pacing only? What are the disadvantages of ventricular pacing?

Atrial pacing only increases cardiac output by 26% over the cardiac output of ventricular pacing only because atrial contraction contributes to approximately 15% to 25% of the diastolic filling of the ventricle. It has been shown that coronary blood flow increases and coronary resistance decreases during atrial pacing only. Atrial pacing has also been shown to reduce the incidence of atrial fibrillation. Atrial pacing only is seldomly used in the United States and often is implanted with the addition of a ventricular pacing lead in the event of AV block.

Ventricular pacing, occurring individually or sequentially with atrial pacing, has been shown to result in dyssynchronous left ventricular electrical activation and mechanical contraction. Under normal circumstances, electrical activation along the His-Purkinje system results in a near simultaneous activation of the entire left ventricle. This allows for efficient contraction and is said to be synchronous. When ventricular pacing is introduced, this results in activation of the right ventricle first, followed by passive activation of the left ventricular free wall. This form of contraction is said to be dyssynchronous and has been shown to potentially worsen congestive heart failure and left ventricular ejection fraction. Prior studies have shown that individuals at greatest risk for developing reductions in ejection fraction from right ventricular pacing are those who exhibit ventricular pacing greater than 40% of the time. Further, individuals at greatest risk for worsening congestive heart failure are those who not only have a pacing greater than 40% of the time, but also have an ejection fraction less than 40% at the time of pacemaker implantation.

Healey JS, Toff WD, Lamas GA, et al. Cardiovascular outcomes with atrial-based pacing compared with ventricular pacing: meta-analysis of randomized trials, using individual patient data. *Circulation*. 2006;114:11–17.

Sweeney MO, Hellkamp AS, Ellenbogen KA, et al. Adverse effect of ventricular pacing on heart failure and atrial fibrillation among patients with normal baseline QRS duration in a clinical trial of pacemaker therapy for sinus node dysfunction. *Circulation*. 2003;107:2932–2937.

A.9. What are the indications for and complications associated with AV sequential PPMs?

When ventricular pacing alone cannot maintain adequate cardiac output and atrial pacing alone is not justified, as in complete AV block, AV sequential pacing is indicated. Because of the success of transvenous leads, bioengineering advances such as thinner polyurethane insulation and improved device programmability, the indications for dual-chamber pacing, have broadened. It can be used for sick sinus syndrome and all degrees of heart block. PPMs programmed to DDD pacing are the ultimate form of physiologic pacing. Programmable features include the mode of pacing, the AV delay, the maximum atrial rate that the ventricle will follow (atrial tracking), and the minimum atrial rate for sensing at which atrial pacing commences. The major advantage of such pacing

is the ability to significantly increase the cardiac output under extreme stress and a reduced incidence of atrial fibrillation development. Historically, the major disadvantage of DDD pacing has been the possibility of pacemaker-mediated tachycardia. More recently, another disadvantage recognized has been the development of ventricular dyssynchrony (see section A.8) as a result of ventricular pacing. Long-term follow-up of patients with dual-chamber pacemakers demonstrated reductions in left ventricular ejection fractions when compared to atrial pacing alone, especially in the setting of preexisting left ventricular dysfunction.

Libby P, Bonow RO, Mann DL, et al., eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 8th ed. Philadelphia: Saunders; 2008:838–839, 854–858.

Nielsen JC, Bottcher M, Nielsen TT, et al. Regional myocardial blood flow in patients with sick sinus syndrome randomized to long-term single chamber atrial or dual chamber pacing: effect of pacing mode and rate. *J Am Coll Cardiol*. 2000;35:1453–1461.

Sweeney MO, Hellkamp AS, Ellenbogen KA, et al. Adverse effect of ventricular pacing on heart failure and atrial fibrillation among patients with normal baseline QRS duration in a clinical trial of pacemaker therapy for sinus node dysfunction. *Circulation*. 2003;107:2932–2937.

A.10. How would you know if the patient's PPM was atrially, ventricularly, or atrioventricularly sequentially pacing?

In atrial pacing, an electrical spike often appears before the P wave and the QRS complex is usually normal, provided there is normal intrinsic AV conduction. One may need to adjust the monitor so that pacing spikes are accentuated and can readily be seen. In ventricular pacing, the electrical spike is followed immediately by a widened left bundle branch block–like QRS complex. In AV sequential pacing, there are two spikes, one before the P wave and another preceding the QRS complex.

Libby P, Bonow RO, Mann DL, et al., eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 8th ed. Philadelphia: Saunders; 2008:837–846.

A.11. What is the maximum amount of energy that a modern PPM can provide in terms of pulse amplitude and pulse width?

In order to successfully pace the heart, the PPM must provide enough energy to allow for cardiac depolarization. Energy is a direct function of the amount of voltage produced (pulse amplitude) and the duration of time the voltage is delivered (pulse width). Although small variations exist among all modern PPMs, the maximum pulse amplitude or output of stimulation usually is 7.5 volts (V). The maximum pulse width or the duration of stimulation is usually 1.5 msec.

Libby P, Bonow RO, Mann DL, et al., eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 8th ed. Philadelphia: Saunders; 2008:841–842.

A.12. During a new PPM implantation, what are the acceptable values for modern pacemaker leads in terms of pacing thresholds, amplitude of sensed intrinsic activity and impedance?

Because current PPMs have a maximal pacing output of 7.5 V at 1.5 msec, the pacing threshold cannot exceed the previously mentioned values. In fact, fluctuations in the pacing threshold can occur during the first few weeks after a pacing lead has

been implanted. There is an initial sharp rise in the pacing threshold during the first 2 weeks because of tissue reaction around the tip of the electrode despite the presence of steroid embedded at the tip. The threshold then returns to levels similar to what were seen at the time of implant. As a result, all device manufacturers recommend that the pacing output be at least two times the voltage of the threshold value or three times the pulse width of the threshold value. In the chronic state, pacing thresholds remain essentially at the same level in 80% of patients. For the ventricular lead, the intrinsic R waves should be at least 5 to 6 mV in amplitude. For the atrial lead, the intrinsic P waves should be at least 1mV in amplitude. Impedances for atrial or ventricular leads should be between 250 and 1300 ohms, depending on the type of lead implanted. Acceptable threshold values for the atrial or ventricular lead are typically those below 2V at 0.4msec.

A.13. What is a biventricular PPM or CRT device? What are the indications for such a device?

It has long been recognized that individuals with interventricular conduction abnormalities have a predilection toward impaired left ventricular systolic function. In fact, one of the more common interventricular conduction delays seen in patients with congestive heart failure is left bundle branch block (LBBB). On a mechanistic level, individuals with LBBB demonstrate ventricular dyssynchrony, a phenomenon whereby the left ventricle contracts in a stepwise process. Unlike normal individuals where the left ventricular septum and the left ventricular lateral free wall contract nearly simultaneously, patients with LBBB have a delay in the activation of the left lateral free wall. As a result, there is marked impairment in left ventricular systolic function and increased myocardial work and oxygen consumption. One approach to correct this dyssynchrony is to "resynchronize" the heart through the use of a biventricular pacemaker/ICD. These devices are capable of pacing both the left ventricular septum (through a pacemaker lead in the right ventricle) and the left ventricular lateral free wall simultaneously (through a pacemaker lead in the coronary sinus), thereby allowing for activation of the entire left ventricle at the same time. Candidates for implantation of a biventricular device include individuals with severe cardiomyopathy (ejection fraction 35% or less), wide QRS complex greater than 120 milliseconds with moderate to severe heart failure symptoms despite optimal medical therapy.

Jarcho JA. Biventricular pacing. *N Engl J Med.* 2006;355:288–294.

A.14. What are the usual life spans of PPMs and ICDs?

Lithium-powered pacemakers can last 5 to 10 years for dual-chamber pacing and 7 to 12 years for single-chamber pacing. The silver-vanadium oxide batteries used in ICDs typically last for 5 to 8 years.

Atlee JL, Bernstein AD. Cardiac rhythm management devices (part I). *Anesthesiology.* 2001;95:1265–1280.

Ellenbogen KA, Kay GN, Lau CP, et al., eds. *Clinical Cardiac Pacing, Defibrillation and Resynchronization Therapy*. 3rd ed. Philadelphia: Elsevier; 2007:235–259.

A.15. What is an ICD? How does it work?

An ICD system consists of a pulse generator and leads for tachyarrhythmia detection and therapy. ICDs provide antitachycardia and antibradycardia pacing; synchronized (cardioversion) or nonsynchronized (defibrillation) shocks; telemetry;

and diagnostics including stored event electrograms and history logs. Essentially, the pulse generator is a self-powered computer within a hermetically sealed titanium casing (can). A battery with high power density is used to power the pulse generator, circuitry, and aluminum electrolytic storage capacitors. Most ICD designs use two capacitors in series to achieve a maximum voltage for defibrillation. A major challenge in ICD design is the large range of voltages that must be controlled in a very small package. Modern devices can charge up to 41 joules of energy.

Modern ICDs use transvenous lead systems for sensing, pacing, and shocks. Epicardial leads are still used in infants and small children. Ventricular demand pacing for bradycardia is a standard feature of all ICDs. Modern day ICDs have all the capabilities of modern day pacemakers, including rate-adaptive pacing and automatic mode switching. The response of ICDs to magnets differs from that of a pacemaker (see section C.8).

Current ICDs have many programmable features, but essentially they measure each cardiac R-R interval and categorize the rate as normal, too fast (short R-R interval), or too slow. When the device detects a sufficient number of short R-R intervals within a period of time (all programmable), it will declare a tachycardia episode. The internal computer will decide between antitachycardia pacing (less energy use, better tolerated by patient) and shock based on its programmed algorithm. If shock is chosen, an internal capacitor is charged that takes approximately 5 to 13 seconds depending on the amount of energy to be delivered and age of the device. Most devices are programmed to reconfirm ventricular tachycardia or ventricular fibrillation after charging to prevent inappropriate shock therapy. Typically, ICDs deliver no more than six shocks per episode. Once therapy is delivered, the ICD will redetect to determine whether or not the therapy successfully terminated the arrhythmia. A tachycardia episode is considered terminated when sinus rhythm has been restored for a certain period (varies by manufacturer).

Atlee JL, Bernstein AD. Cardiac rhythm management devices (part I). *Anesthesiology*. 2001;95:1265–1280.

Libby P, Bonow RO, Mann DL, et al., eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 8th ed. Philadelphia: Saunders; 2008:847–852.

A.16. What are the indications for ICDs?

Initially, ICDs were indicated for hemodynamically significant ventricular tachycardia or ventricular fibrillation. Newer indications include the following and continue to evolve:

- Survivors of cardiac arrest because of ventricular tachycardia/ventricular fibrillation not resulting from a transient or reversible cause
- Spontaneous or induced at electrophysiology study sustained ventricular tachycardia in the presence of structural heart disease
- Syncope of undetermined origin with clinically relevant, hemodynamically significant sustained ventricular tachycardia or ventricular fibrillation-induced at electrophysiology study
- Ischemic cardiomyopathy (ejection fraction ≤30%) without a recent myocardial infarction (within the last 40 days) or revascularization in the past 3 months
- Ischemic or nonischemic dilated cardiomyopathy (ejection fraction ≤35%) with NYHA class II or III heart failure symptoms
- Brugada syndrome—RBBB and ST segment elevation leads V_1 to V_3
- Arrhythmogenic right ventricular dysplasia
- Long and short QT syndromes
- Hypertrophic obstructive cardiomyopathy

Table 7.2 NASPE/BPEG Generic Defibrillator (NBD) Code

LETTER I SHOCK CHAMBER(S)	LETTER II ANTITACHYCARDIA PACING CHAMBER(S)	LETTER III TACHYCARDIA DETECTION	LETTER IV ANTIBRADYCARDIA PACING CHAMBER(S)
O = None	O = None	E = Electrogram	O = None
A = Atrium	A = Atrium	H = Hemodynamic	A = Atrium
V = Ventricle	V = Ventricle	(not yet available)	V = Ventricle
D = Dual (A + V)	D = Dual (A + V)		D = Dual (A + V)

BPEG, British Pacing and Electrophysiology Group; NASPE, North American Society of Pacing and Electrophysiology; NBD, NASPE/BPEC generic defibrillator.

Epstein AE, DiMarco JP, Ellenbogen KA, et al. ACC/AHA/HRS 2008 Guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation.* 2008;117:e350–e408.

A.17. What is the NASPE and BPEG generic defibrillator (NBD) code?

Like pacemakers, ICDs have a generic code to indicate lead placement and function. The NBD code is shown in Table 7.2. The most robust form of identification, referred to as the "label form," replaces the fourth letter of the NBD with the appropriate generic pacemaker code.

Practice advisory for the perioperative management of patients with cardiac implantable electronic devices: pacemakers and implantable cardioverter-defibrillators: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Cardiac Implantable Electronic Devices. *Anesthesiology.* 2011;114:247–261.

B. Preoperative Evaluation and Preparation

B.1. How would you preoperatively evaluate the patient described earlier?

Preoperative evaluation should include the routine systemic workup, paying particular attention to cardiovascular disorders. The comprehensive evaluation includes complete blood count, urinalysis, coagulation screening with prothrombin time and partial thromboplastin time, serum electrolytes, blood urea nitrogen, blood sugar, chest radiograph, and ECG. Special attention should be paid to the history, symptoms, and signs of myocardial infarction, congestive heart failure, and arrhythmia. Serum electrolytes, especially potassium level, must be in the normal range. For the patient with a CIED, recent guidelines have recommended that all CIEDs be properly interrogated within 3 to 6 months before surgery. This evaluation should include the following:

- Establish whether a patient has a CIED
- Define the type of CIED
- Determine dependency on pacing function of the CIED
- Determine CIED function and programming details

- Determine magnet behavior and whether CIED requires reprogramming on the day of surgery to avoid inappropriate device behavior from EMI.

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Salukhe TV, Dob D. Pacemakers and defibrillators: anesthetic implications. *Br J Anesth*. 2004;93:95–104.

The Heart Rhythm Society Expert Consensus Statement on the perioperative management of patients with implantable defibrillators, pacemakers and arrhythmia monitors: Facilities and patient management. Crossley GH, Poole JE, Rozner MA, et al. Heart Rhythm 2011; in press.

B.2. How do you determine whether the patient has a cardiac implantable electronic device (CIED) and define what type of CIED?

Determining whether a patient has a CIED should be based on (1) a focused history including but not limited to the patient interview, medical records review, review of available chest radiograph, ECG, or any available monitor or rhythm strip information, and (2) a focused physical examination (e.g., checking for scars, palpating for device).

Defining the type of device is accomplished by (1) obtaining the manufacturer's identification card from the patient or other source, (2) ordering chest radiography studies if no other data are available, or (3) referring to supplemental resources (e.g., manufacturers' databases, pacemaker clinic records, consultation with a cardiologist).

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B.3. How do you determine whether the patient is dependent on pacing function of the CIED?

CIED dependency for pacemaking function may be determined by one or more of the following: (1) a verbal history or an indication in the medical record that the patient has experienced a bradyarrhythmia that has caused syncope or other symptoms requiring CIED implantation, (2) a history of successful AV nodal ablation that resulted in CIED placement, or (3) a CIED evaluation that shows clinically evidenced hemodynamic compromise when the pacemaking function of the CIED is temporarily programmed to VVI pacing mode at the lowest programmable rate.

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B.4. How do you know if the implanted PPM or ICD is working?

The CIED function is ideally assessed by interrogating the device. If interrogating the device is not an option, one can slow the intrinsic heart rate to a rate below that

of the pacemaker by carotid massage or the Valsalva maneuver. Carotid massage to slow the heart rate should be used cautiously because it could result in an arteriosclerotic plaque embolizing to the cerebral circulation. If the rate does not slow down enough for the pacemaker to take over the ventricle, the device can be tested by placing a magnet over it that will temporarily program it to a fixed-rate pacing mode. In this mode, pacing spikes march through the rhythm strip with no regard for the intrinsic electrical activity of the heart. The rate at which the pacemaker will pace in the presence of a magnet varies among device manufacturers and is dependent on the battery life. Once the magnet is removed, the device returns to its normal programming.

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B.5. What information would you like to obtain from interrogating this device?

Device interrogations provide information on the status and current programmed settings of a PPM or ICD. The important primary information for anesthesiologists include (1) battery life, (2) programmed pacing mode such as VVIR, DDDR, (3) pacemaker dependency, (4) intrinsic rhythm, (5) behavior to a magnet, (6) prior recorded arrhythmic events, and (7) pacemaker lead parameters (including pacing threshold, ability to sense intrinsic activity, and lead impedance).

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B.6. How do you preoperatively prepare the patient for surgery and anesthesia?

Preparation for patient safety and proper maintenance of the device during a procedure includes the following:

- Determining whether EMI is likely to occur during the planned procedure, as well as the location of the EMI
- Properly positioning the electrocautery grounding pad so the path of conduction across the device is minimized to the fullest extent
- Determining whether reprogramming the CIED pacemaking function to an asynchronous pacing mode or disabling any special algorithms, including rate-adaptive functions, is needed
- Suspending antitachyarrhythmia functions if present
- Advising the surgeon performing the procedure to minimize prolonged bursts or monopolar cautery or use other less interfering sources of energy including bipolar electrocautery or ultrasonic (harmonic) scalpel
- Ensuring the availability of temporary pacing and defibrillation equipment
- Evaluating the possible effects of anesthetic techniques and of the procedure on CIED function and patient–CIED interactions.

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B.7. Would you recommend reprogramming this device to asynchronously pace before surgery? What would you recommend regarding the ICD functions of the device?

Given the number of patients with CIEDs, recommending that all patients undergo reprogramming immediately before surgery is untenable and would significantly compromise perisurgical throughput. Moreover, reports have described individuals with ICDs or PPMs who later expired because the device was not reactivated before discharge after surgery. These issues raise the need for proper triaging of patients who truly need their devices reprogrammed before surgery. The patient in this example has a CRT-implantable cardioverter defibrillator because of sick sinus syndrome, intermittent heart block, and ventricular tachycardia. It is likely that the patient is functionally dependent on the CIED. Furthermore, the location of the EMI delivered in this case is close to the device system and therefore would likely result in inappropriate inhibition of pacing or sensing of EMI that the device would inappropriately mark as ventricular fibrillation. Given functional dependency on the device and the location of the EMI delivered, reprogramming the device would be recommended to deactivate the ICD and pace asynchronously before surgery for the following reasons:

- Electrocautery during surgery may inhibit pacing function.
- A magnet cannot convert the pacemaker in an ICD system to asynchronous mode pacing. A magnet placed over an ICD only disables tachycardia detection and therapy of the ICD. This is true of all devices used in the United States. One notable exception are ICDs manufactured by ELA Medical (Cedex, France), which, in the presence of a magnet, will not only disable tachycardia detection therapy but also convert pacing to a fixed rate at 96 beats per minute.

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C. Intraoperative Management

C.1. How would you monitor this patient?

Intraoperative monitoring should include both continuous ECG and continuous peripheral pulse monitoring. Peripheral pulse can be monitored by palpation of the pulse, auscultation of heart sounds, pulse plethysmography or oximetry, a tracing of arterial wave form, or ultrasound peripheral pulse monitoring.

Arterial line and central venous pressure or pulmonary artery pressure monitoring may be used only if the patient has poor ventricular function. The artifact filter on the ECG monitor should be disabled to detect the pacing spikes. The ECG monitor should be set in diagnostic mode instead of monitoring mode.

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The Heart Rhythm Society Expert Consensus Statement on the perioperative management of patients with implantable defibrillators, pacemakers and arrhythmia monitors: Facilities and patient management. Crossley GH, Poole JE, Rozner MA, et al. Heart Rhythm 2011; in press.

C.2. What drugs and equipment would you like to have on hand in the operating room?

A complete array of drugs and equipment must be immediately available for cardiopulmonary resuscitation. The minimal requirements include ECG monitor, a transcutaneous external pacing and direct current (DC) defibrillator, and the usual drugs for resuscitation.

Atlee JL, Bernstein AD. Cardiac rhythm management devices (part I). *Anesthesiology*. 2001;95:1265–1280.

Ellenbogen KA, Kay GN, Lau CP, et al., eds. *Clinical Cardiac Pacing, Defibrillation and Resynchronization Therapy*. 3rd ed. Philadelphia: Elsevier; 2007:561–651.

C.3. How would you set up the transcutaneous external pacer and defibrillator?

We prefer applying defibrillating electrodes such as Zoll® Pads to paddles because the electrodes can be placed before surgery at the desirable positions and connected to a defibrillator/pacemaker for pacing and defibrillation. The electrodes should be placed as far (more than 6 in. or 15 cm) from a CIED as possible. The three recommended electrode placements are as follows:

- *Anteroposterior placement*. The right arm (RA) electrode placed under the left scapula and the left leg (LL) electrode at apex of the heart (as shown in Fig. 7.2).
- *Apex-anterior placement*. The RA electrode placed under the right clavicle and the LL electrode at the apex of the heart (Fig. 7.3A).
- *Apex-posterior placement*. The RA electrode placed over the right scapula and the LL electrode at the apex of the heart (Fig. 7.3B).

It is important to remember that the presence of a CIED should not deter standard resuscitation efforts.

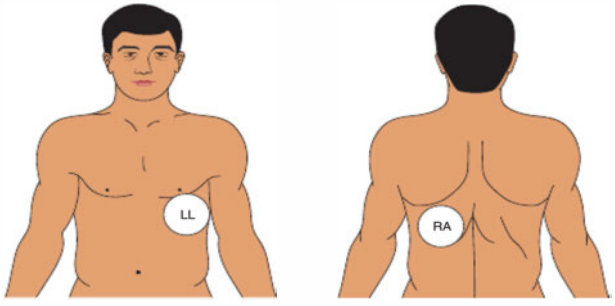

Figure 7.2 Anterior–posterior placement of defibrillating electrodes. The right arm (RA) electrode is placed under the left scapula, and the left leg (LL) electrode is placed at the apex of the heart.

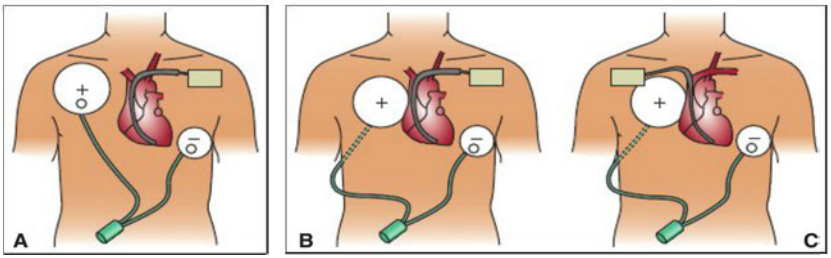

Figure 7.3 Placement of defibrillating electrodes. **A.** Apex–anterior placement with both pads placed anteriorly. **B** and **C.** Apex–posterior placement shown with the device in the left prepectoral region **(B)** and the right pectoral region **(C)**. (Adapted from Ellenbogen KA, Kay GN, Wilkoff BL, eds. *Clinical Cardiac Pacing and Defibrillation*. 2nd ed. Philadelphia: Saunders; 2000:944.)

Stone KR, McPherson CA. Assessment and management of patients with pacemakers and implantable cardioverter defibrillator. *Crit Care Med*. 2004;32(suppl):S155–S165.

C.4. Had this patient's ICD been implanted the day before surgery, would you consider avoiding certain inhalational gases for anesthesia?

It has been reported that nitrous oxide could cause pacemaker malfunction by increasing gas in the prepectoral pacemaker pocket. Despite air evacuation with antibiotic solution before closure of the prepectoral pocket, a small amount of air remains entrapped in the pocket. In general, this small amount of air should have no clinical significance. Nitrous oxide is 35 times more soluble in blood than nitrogen. When nitrous oxide is used for anesthesia, the amount of nitrous oxide diffused from blood to the air pocket is much more than the amount of nitrogen diffused from the air pocket to blood. Therefore, this causes an expansion of the gas in the pocket that leads to loss of anodal contact and pacing system malfunction. It is advisable not to use nitrous oxide in a patient with a newly implanted pacemaker.

Lamas GA, Rebecca GS, Braunwald NS, et al. Pacemaker malfunction after nitrous oxide anesthesia. *Am J Cardiol*. 1985;56:995.

C.5. Electromagnetic interference (EMI) from electrocautery results in significant noise on your cardiac monitor. You recall that EMI also can inhibit pacing function from the PPM. In this pacemaker-dependent patient, how can you determine whether inappropriate inhibition of the PPM is occurring?

During electrocautery, the ECG is frequently useless because of interference. The best monitor available to determine if inhibition is taking place is a hand on the pulse. The precordial or esophageal stethoscope, pulse oximeter, or blood pressure is also acceptable.

Practice advisory for the perioperative management of patients with cardiac implantable electronic devices: pacemakers and implantable cardioverter-defibrillators: an updated report by the American Society of Anesthesiologists task force on perioperative management of patients with cardiac implantable electronic devices. *Anesthesiology*. 2011;114:247–261.

C.6. What are the potential responses of pacemakers and ICDs to electrocautery?

The responses of pacemakers to electrocautery or other EMI include the following:

- Inhibition of pacing
- Asynchronous pacing
- Reset to backup mode
- Myocardial burns, rare
- Ventricular fibrillation, rare

The responses of ICDs include the following:

- Inhibition of pacing
- Asynchronous pacing
- Inappropriate tachy therapy
- Inhibition of tachy therapy

Salukhe TV, Dob D. Pacemakers and defibrillators: anesthetic implications. *Br J Anesth.* 2004;93:95–104.

Stone KR, McPherson CA. Assessment and management of patients with pacemakers and implantable cardioverter defibrillator. *Crit Care Med.* 2004;32(suppl):S155–S165.

C.7. How would you prevent the effects of EMI on the pacemaker or ICD from the electrocautery?

The safest way to prevent intraoperative EMI response is appropriate reprogramming. The following precautions should be taken to minimize the effects of electrocautery:

- Place the cautery grounding plate as close to the operative site and as far from the CIED as possible to make sure that the current pathway does not pass through or near the CIED system. For some cases, the grounding plate might need to be placed on a site different from the thigh (e.g., the superior posterior aspect of the shoulder contralateral to the CIED generator position for a head and neck case).
- Do not use cautery within 15 cm of the pacemaker because it may interfere with the battery circuitry. If in contact with a break in the insulation of the electrode, it may cauterize the myocardium at the electrode tip, rendering it insensitive to pacing impulses.
- Limit cautery use to 1-second bursts every 10 seconds to prevent repetitive asystolic periods (if possible).
- If the pacemaker is inhibited by the cautery, place a high-powered magnet over the demand nonprogrammable pacemaker to convert it to fixed-rate mode.
- Using bipolar electrocautery forceps or ultrasonic (harmonic) scalpel reduces EMI.

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Salukhe TV, Dob D. Pacemakers and defibrillators: anesthetic implications. *Br J Anesth.* 2004;93:95–104.

Stone KR, McPherson CA. Assessment and management of patients with pacemakers and implantable cardioverter defibrillator. *Crit Care Med.* 2004;32(suppl):S155–S165.

C.8. What are the effects of a magnet over pacemakers and ICDs?

The effect of placing a magnet over a pacemaker or ICD can vary quite considerably depending on the device manufacturer, model, and individual programmed modes. This information may be obtained by consulting the device manufacturer's representative. Most pacemakers will switch to a fixed-rate pacing mode when a magnet is placed. However, the response of a pacemaker to a magnet placement may also include the following:

- Asynchronous pacing without rate responsiveness
- No response
- Brief (10 to 100 beats) asynchronous pacing
- Continuous or transient loss of pacing

The response of an ICD to magnet placement is different from the response of a pacemaker. Magnets will disable tachyarrhythmia detection and therapy that, except in some Guidant-Boston Scientific devices, are reenabled when the magnet is removed. Magnets generally will, with a few exceptions, not affect the pacing mode or rate of ICDs. Therefore, the pacemaker in an ICD can be inappropriately inhibited by electrocautery even when a magnet is placed.

It is important to remember that some early generation Guidant-Boston Scientific ICDs are permanently disabled when a magnet is placed for more than 30 seconds. The ICD will not be reactivated when the magnet is removed. To reactivate the Guidant-Boston Scientific ICDs, the magnet has to be reapplied over the ICD for more than 30 seconds and then removed. If a magnet is to be used during surgery, the magnet effects should be tested in the operating room before surgery to ensure that the desired effects will occur during surgery.

Salukhe TV, Dob D. Pacemakers and defibrillators: anesthetic implications. *Br J Anesth.* 2004;93:95–104.

Stone KR, McPherson CA. Assessment and management of patients with pacemakers and implantable cardioverter defibrillator. *Crit Care Med.* 2004;32(suppl):S155–S165.

C.9. In the middle of surgery, the patient developed ventricular tachycardia. What would you do?

For a patient with an ICD and magnet-disabled therapies:

- Advise the surgeon performing the procedure to terminate all sources of EMI.
- Remove the magnet to reenable antitachycardia therapies.
- Observe the patient and the monitors for appropriate CIED therapy. This can be delayed for as long as 10 to 12 seconds as the ICD is charging.
- If the activities mentioned in the preceding text do not restore ICD function, proceed with emergency external defibrillation.

For a patient with an ICD and programming-disabled therapies:

- Advise individual performing the procedure to terminate all sources of EMI while magnet is removed.
- Reenable therapies through programming if the programmer is immediately available and ready to be used.
- Observe the patient and the monitors for appropriate CIED therapy.
- If the activities mentioned in the preceding text do not restore ICD function, proceed with emergency external defibrillation.

For external defibrillation (see also section C.3):

- Position defibrillation/cardioversion pads or paddles as far as possible from the CIED generator.

- If it is technically impossible to place the pads or paddles in locations that help to protect the CIED, defibrillate/cardiovert the patient in the quickest possible way and be prepared to provide pacing through other routes.
- Use a clinically appropriate energy output.

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C.10. What precautions should be taken when a patient with a CIED is undergoing extracorporeal shock wave lithotripsy (ESWL)?

ESWL is no longer contraindicated for patients with pacemakers. The only exception to this general statement is the abdominally placed pacemaker generators. Because these generators are in the blast path of the shock wave, such patients should not be treated with ESWL. Nevertheless, most transvenous pacemaker generators are placed in a pectoral location that is at a safe distance from the blast path. Consider preoperative disabling of atrial pacing if the lithotripsy system triggers on the R wave. Avoid focusing the lithotripsy beam near the pulse generator.

Although most pacemakers are not affected by ESWL, sometimes it may cause pacemaker malfunctions that include the following:

- Switching to magnet mode
- Reaching upper rate limit
- Pacing irregularity
- Oversensing of asynchronous shocks
- Damage to rate-sensing piezoelectric crystal
- Intermittent inhibition of ventricular output in dual-chamber pacemaker
- EMI

There may be a rate increase in a rate-response (adaptive) pacemaker after ESWL shocks. Therefore, special precautions should be taken preoperatively. The type of pacemaker, indications for its placement, degree of patient dependence, and pacemaker programmability must be determined before lithotripsy. A dedicated pacemaker programmer should be available in the lithotripsy suite should pacemaker malfunction be caused by the shock waves. In addition, an alternative means of pacing, such as transcutaneous pacing, should also be available in case the pacemaker becomes permanently damaged. Low-energy shock waves (less than 16 kV) should be used initially; then the energy level is gradually increased while pacemaker function is monitored carefully. It is best to disable tachycardia detection of an ICD during ESWL and to thoroughly test the ICD following the procedure.

Atlee JL, Bernstein AD. Cardiac rhythm management devices (part I). *Anesthesiology.* 2001; 95:1265–1280.

Practice advisory for the perioperative management of patients with cardiac implantable electronic devices: pacemakers and implantable cardioverter-defibrillators: an updated report by the American Society of Anesthesiologists task force on perioperative management of patients with cardiac implantable electronic devices. *Anesthesiology.* 2011;114:247–261.

C.11. Is electroconvulsive therapy (ECT) contraindicated in patients with pacemakers or ICDs?

It is advisable to consult with the ordering physician, the patient's cardiologist, a cardiac rhythm management device (CIED) service, or the device manufacturer. ECT appears safe for patients with pacemakers or ICDs because little current flows within the heart due to the high impedance of body tissues. Nevertheless, the seizure and

succinylcholine fasciculations may generate sufficient myopotentials for pacemaker inhibition (unipolar devices) or ventricular tracking (adaptive-rate devices). Therefore, it is advisable to program the pacemaker to a nonsensing (asynchronous) mode for pacemaker-dependent patients either by reprogramming prior to the procedure or using a magnet during the case. It is also important to keep in mind that a magnet placed over an ICD will only disable tachytherapies and will not cause the ICD to pace asynchronously. An external pacemaker should also be available. Current guidelines also suggest that all ICDs should be programmed so that tachycardia detection is disabled before ECT and reprogrammed to its original programmed parameters prior to discharge.

Atlee JL, Bernstein AD. Cardiac rhythm management devices (part I). *Anesthesiology*. 2001;95:1265–1280.

Practice advisory for the perioperative management of patients with cardiac implantable electronic devices: pacemakers and implantable cardioverter-defibrillators: an updated report by the American Society of Anesthesiologists task force on perioperative management of patients with cardiac implantable electronic devices. *Anesthesiology*. 2011;114:247–261.

Stone KR, McPherson CA. Assessment and management of patients with pacemakers and implantable cardioverter defibrillator. *Crit Care Med*. 2004;32(suppl):S155–S165.

C.12. Is magnetic resonance imaging (MRI) contraindicated in patients with a CIED?

MRI is generally contraindicated in patients with a CIED. If MRI must be performed, consult with the ordering physician, the patient's cardiologist, the diagnostic radiologist, and the CIED manufacturer. MRI can cause rapid pacing, inhibition, resetting of DDD pacemakers, and transient reed switch malfunction with asynchronous pacing. Serious malfunction with no output or rapid pacing may occur because pulsed energy from MRI can enter the lead by capacitive coupling and cause rapid ventricular pacing. Recent studies suggest that MRI may be safe, at least with some models of pacemakers or ICDs, provided the CIED generator and leads are not inside the magnet bore. When MRI is considered absolutely essential, it is reasonable to program the pacemaker to its lowest voltage and pulse width or to OOO mode, provided the patient has an adequate underlying rhythm. The pulse waveform should be closely monitored in pacemaker-dependent patients, and an external pacemaker and defibrillator should be available. Device function must be checked after MRI.

Atlee JL, Berstein AD. Cardiac rhythm management devices (part I). *Anesthesiology*. 2001;95:1265–1280.

Practice advisory for the perioperative management of patients with cardiac implantable electronic devices: pacemakers and implantable cardioverter-defibrillators: an updated report by the American Society of Anesthesiologists task force on perioperative management of patients with cardiac implantable electronic devices. *Anesthesiology*. 2011;114:247–261.

Roguin A, Schwitter J, Vahlhaus C, et al. Magnetic resonance imaging in individuals with cardiovascular implantable electronic devices. *Europace*. 2008;10:336–346.

C.13. What are the precautions during radiofrequency ablation for a patient with a CIED?

- Avoid contact of radiofrequency catheter with the CIED generator and leads
- Radiofrequency current path as far away from the CIED generator and leads as possible
- Discuss these concerns with the operator

Practice advisory for the perioperative management of patients with CIEDs: pacemakers and implantable cardioverter-defibrillators: an updated report by the American Society of Anesthesiologists task force on perioperative management of patients with cardiac implantable electronic devices. *Anesthesiology*. 2011;114:247–261.

D. Postoperative Management

D.1. How would you monitor this patient in the postanesthesia care unit?

Cardiac rate and rhythm should be continuously monitored throughout the immediate postoperative period. Backup pacing capability and cardioversion-defibrillation equipment should be immediately available at all times.

Practice advisory for the perioperative management of patients with cardiac implantable electronic devices: pacemakers and implantable cardioverter-defibrillators: an updated report by the American Society of Anesthesiologists task force on perioperative management of patients with cardiac implantable electronic devices. *Anesthesiology*. 2011;114:247–261.

The Heart Rhythm Society Expert Consensus Statement on the perioperative management of patients with implantable defibrillators, pacemakers and arrhythmia monitors: Facilities and patient management. Crossley GH, Poole JE, Rozner MA, et al. Heart Rhythm 2011; in press.

D.2. How would you confirm that the CIED is functioning properly after surgery?

Postoperative interrogation and restoration of CIED function are basic elements of postoperative management. But given the robustness of modern devices, not all CIEDs require postoperative interrogation before discharge, especially in cases in which the EMI is remote from the device system. CIEDs that should be interrogated postoperatively before discharge include:

- CIEDs that were reprogrammed or deactivated before surgery so that baseline settings can be restored
- Patients who underwent hemodynamically embarrassing surgeries such as cardiac surgery or significant vascular surgery
- Patients who experienced significant intraoperative events, including cardiac arrest, requiring temporary pacing or cardiopulmonary resuscitation and/or tachyarrhythmias requiring external electrical cardioversion during surgery

All other individuals should have their devices evaluated as an outpatient within the next 3 months.

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CHAPTER 8

Thoracoabdominal Aortic Aneurysms

J. Mauricio Del Rio, Jeffrey G. Gaca, Mani A. Daneshmand, and Madhav Swaminathan

A 67-YEAR-OLD WOMAN

presents for evaluation and surgical treatment of a thoracoabdominal aortic aneurysm (TAAA). The patient's past medical history is significant for a type III aortic dissection 8 years ago, hypertension, chronic obstructive pulmonary disease (COPD), smoking (50-pack years), and stage III chronic kidney disease. The patient currently complains of intermittent back pain. Computed tomography (CT) reveals a 9-cm TAAA originating just distal to the left subclavian artery that extends to the iliac bifurcation. Chest radiograph shows thoracic aortic aneurysmal dilation, with displacement of the left bronchial mainstem. Echocardiogram shows concentric left ventricular hypertrophy and a normal ejection fraction. Laboratory studies indicate hemoglobin, 9.3 g/dL; hematocrit, 37%; blood urea nitrogen, 22 mg/dL; and creatinine, 1.9 mg/dL.

A. Medical Disease and Differential Diagnosis

1. What are the different types of aortic pathologies?
2. What is the pathogenesis of aortic aneurysms?
3. How are thoracic aortic dissections classified?
4. How are TAAAs classified?
5. Describe the natural history and clinical presentation of TAAAs.
6. What are the indications for and timing of surgical intervention for TAAAs? Describe the medical management.

B. Preoperative Evaluation and Preparation

1. How should TAAAs be surgically evaluated?
2. Describe the preoperative evaluation and risk assessment of the patient scheduled for TAAA repair.
3. Describe the spinal cord blood supply.

C. Intraoperative Management

1. What hemodynamic monitors should be used for the patient undergoing TAAA repair?
2. What are the possible blood conservation techniques and blood product requirements for TAAA repair?
3. Describe the surgical approach to TAAA repair.
4. What are the specific considerations for anesthetic management of the patient for TAAA repair?
5. What major organ systems are threatened during TAAA repair?
6. What strategies are used for spinal cord protection?
7. How do you detect spinal cord ischemia?
8. What strategies are used for mesenteric and renal preservation?
9. Describe the pathophysiology of aortic clamping and unclamping.

D. Postoperative Management

1. What are the potential complications of TAAA repair?

E. Anesthesia for Endovascular TAAA Repair

1. Which patients are candidates for endovascular TAAA repair?
2. What are the surgical steps for endovascular TAAA repair?
3. What are the specific anesthetic considerations for endovascular TAAA repair?
4. What are the potential complications of endovascular TAAA repair?

A. Medical Disease and Differential Diagnosis

A.1. What are the different types of aortic pathologies?

The major disease processes affecting the aorta are aneurysms and dissections. An aneurysm is a localized abnormal dilation of a blood vessel. A true aortic aneurysm is defined as a localized dilation of the aorta, 1.5 times the normal diameter (for anatomic segment, age, gender, and body size), which includes an intact attenuation of all three-vessel layers (i.e., the intima, media, and adventitia). In contrast, a pseudoaneurysm is a defect in the vascular wall leading to an extravascular hematoma that freely communicates with the intravascular space. Aneurysms can also be classified according to morphology and location.

The morphologic classification distinguishes true aneurysms into *fusiform* and *saccular*. Fusiform aneurysms involve diffuse, circumferential dilation of a long vascular segment. Saccular aneurysms are spherical outpouchings that involve only a portion of the vessel wall (Fig. 8.1). Fusiform aneurysms are much more common than saccular ones, and both of these types are not specific for any disease or clinical manifestation.

Apart from shape, aortic aneurysms may also be classified according to the segment involved as thoracic aneurysms (which include the ascending or descending aorta in the thoracic cavity), and thoracoabdominal or abdominal (involving the infrarenal abdominal aorta). Ascending aortic aneurysms are typically fusiform and may extend into the aortic arch. Descending aortic aneurysms start below the ligamentum arteriosum and often begin distal to the origin of the left subclavian artery. These aneurysms are typically fusiform and can extend to the level of the abdominal aorta. Chronic aneurysms tend to be larger, which, over time, develop sluggish flow, leading to intraluminal thrombus formation (Fig. 8.2). The location of the aneurysm has clinical and therapeutic implications because the pathogenesis and natural history of ascending and descending aortic aneurysms are different.

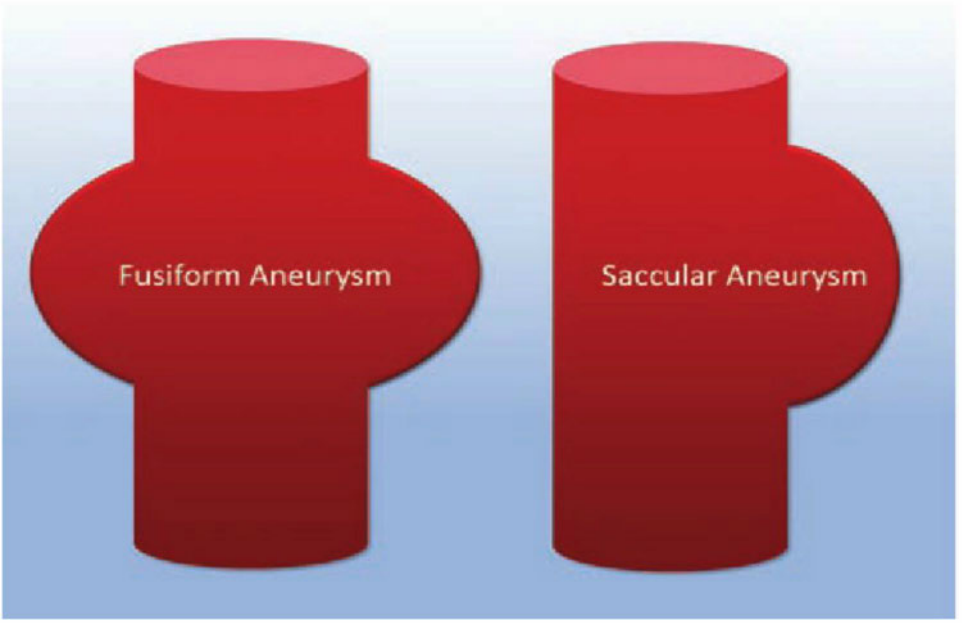

Figure 8.1 Illustration of two different morphologic forms of aortic aneurysms. The figure on the left shows a circumferential dilation of the aortic wall and represents a *fusiform* aneurysm, while the figure on the right shows a localized dilation, termed a *saccular* aneurysm.

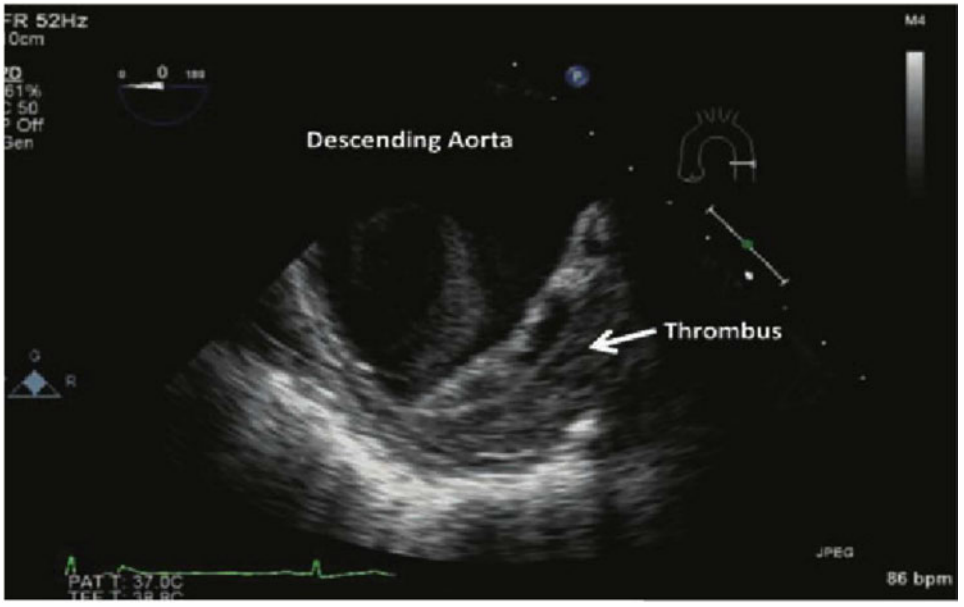

Figure 8.2 Transesophageal echocardiographic image of the descending thoracic aorta demonstrating a large aneurysm with an intraluminal thrombus.

TAAAs have features of both thoracic and abdominal aneurysms and constitute only about 3% of all aortic aneurysms. TAAAs are considered separately because of extensive aortic involvement and special considerations required for surgical repair.

An aortic dissection presents when blood enters the arterial wall through an intimal tear, causing a hematoma that propagates longitudinally between the laminar planes of the media forming a blood-filled channel within the aortic wall. Aortic dissections can rupture through the adventitia causing massive hemorrhage, or they could reenter the lumen through a second intimal tear. It is noteworthy that while aortic aneurysms are predisposed to dissection, aortic dissections may or may not be associated with a pre-existing aortic aneurysm. Consequently, the term "dissecting aneurysm" should be avoided. There are two separate variants of aortic dissection: *intramural hematoma* and *penetrating aortic ulcer*. The intramural hematoma differs from a typical dissection in that it is located circumferentially around the aortic lumen rather than obliquely across it, and there is no flap defining a true and a false lumen. It is not clear if intramural hematomas arise from a small nondissected intimal tear or from a rupture of vasa vasorum within the aortic wall. Penetrating aortic ulcers (Fig. 8.3) are erosions that enter the aortic wall, disrupting the internal elastic lamina and extend into the media, which can lead to rupture, intramural hematoma, or pseudoaneurysm formation. In some cases, these ulcers can mimic true dissections or initiate them. In general, *hypertension* is the major risk factor for aortic dissection. Although medial degeneration is a common finding, it is not essential for a dissection to occur.

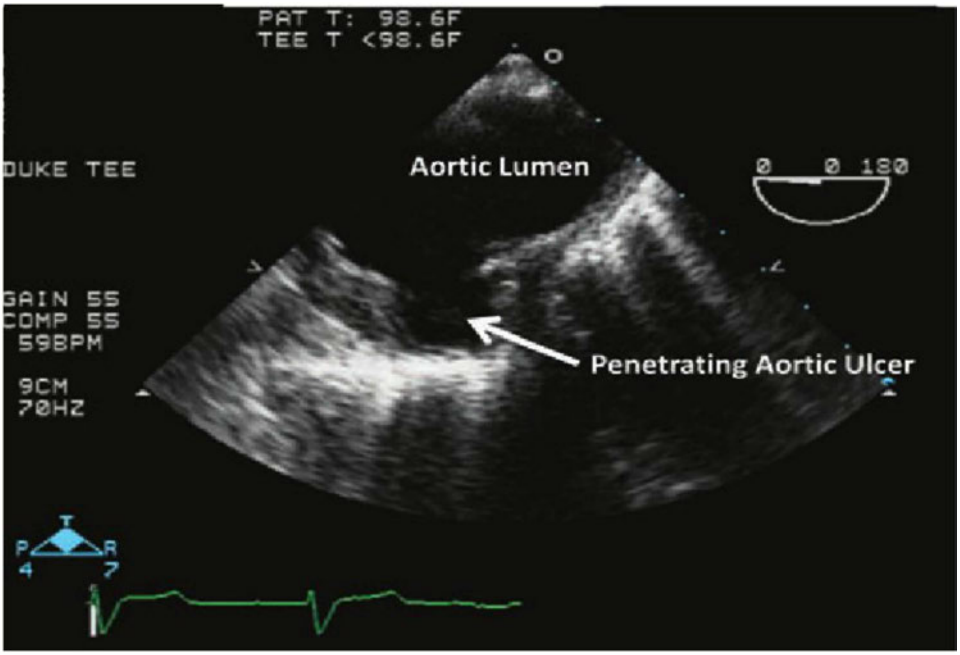

Figure 8.3 Transesophageal echocardiographic image of the descending thoracic aorta demonstrating a penetrating aortic ulcer. Note the overhanging margins of the ulcer, which are characteristic of this condition.

Elefteriades JA. Thoracic aortic aneurysm: reading the enemy's playbook. *Curr Prob Cardiol.* 2008;33:203–277.

Guo DC, Papke CL, He R, et al. Pathogenesis of thoracic and abdominal aortic aneurysms. *Ann NY Acad Sci.* 2006;1085:339–352.

Kumar VS, Abbas AK, Fausto N, et al., eds. *Robbins and Cotran Pathologic Basis of Disease.* 8th ed. Philadelphia: Saunders/Elsevier; 2009.

A.2. What is the pathogenesis of aortic aneurysms?

In general, arteries are dynamically remodeling tissues that maintain their structural and functional integrity by constantly synthesizing, degrading, and repairing their extracellular matrix (ECM). Any alteration in the integrity of the connective tissue can cause weakness of the aortic wall by the following mechanisms:

- *Poor intrinsic quality of vascular wall connective tissue:*
  - In *Marfan syndrome,* the defective synthesis of *fibrillin-1* leads to altered transforming growth factor-beta (TGF-β) activity and weakening of elastic tissue. The aorta progressively dilates as a consequence of remodeling of the media. There are more than 125 identified mutations on the *human fibrillin-1 gene (FBN1).*
  - In *Loeys-Dietz syndrome,* mutations in TGF-β (1 or 2) receptors lead to abnormalities in elastin and collagen II and I. Aneurysms in these patients tend to rupture at smaller sizes. Like Marfan syndrome, it is an autosomal dominant disorder and is subdivided into type 1A, 1B, 2A, and 2B depending on the receptor affected and the location of the mutation. Type 1A is also known as *Furlong disease,* and type 2B was previously known as Marfan syndrome type 2. Clinically, these patients have widely spaced eyes, cleft palate or bifid uvula, and tortuous aneurysmal aortas that are prone to dissection. Many patients with *Loeys-Dietz syndrome* also have bicuspid aortic valves.
  - In *Ehlers-Danlos syndrome,* there is defective type III collagen synthesis.
  - In *severe vitamin C deficiency,* there is altered cross-linking of type III collagen.
- *Imbalance of collagen synthesis and degradation:*
  - The presence of *local inflammatory mediators* in *atherosclerosis* and *vasculitis* promotes an increased production of matrix metalloproteinases by macrophages. These enzymes can degrade all the components of the ECM in the aortic wall. A simultaneous decrease in tissue inhibitor of metalloproteinase expression contributes to ECM degradation.
- *Loss of smooth muscle cells and inappropriate synthesis of noncollagen/nonelastic ECM in the vascular wall:*
  - *Ischemia* of the aortic wall causes degenerative changes, characterized by scarring, loss of smooth muscle cells and elastic fibers, and abnormal deposition of glycosaminoglycans. Ischemia can occur at two levels; when there is atherosclerotic thickening of the intima, there is an increased distance for oxygen and nutrients to diffuse to the inner media. Otherwise, significant narrowing of the vasa vasorum induced by hypertension causes outer media ischemia.
  - The histopathologic changes described above are termed *cystic medial degeneration.* These changes are not specific to any pathology and can be seen in the other entities previously discussed.
- *Polymorphisms of matrix metalloproteinases and/or tissue inhibitor of metalloproteinase genes cause genetic predisposition to aneurysm formation:*
  - There are familial clusters of TAAA and dissection referred as *familial thoracic aortic aneurysm syndrome*. Some mutations in genes encoding for TGF-β receptors 1 and 2 have been identified. Similarly, mutations in the human *myosin heavy chain 11 gene* are responsible for a familial association between thoracoabdominal dissection and patent ductus arteriosus.

- Many ascending thoracic aortic aneurysms are associated with *congenital bicuspid aortic valve*. In the past, it was thought that those aneurysms were caused by "post-stenotic dilatation." In fact, congenital bicuspid aortic valve is associated with a dilated aorta regardless of the presence of hemodynamically significant aortic valve dysfunction. As many as 30% of patients with bicuspid aortic valves will develop aortic dilation. There are inadequate levels of fibrillin-1 during embryogenesis in these patients.
- In *Turner syndrome,* there is association with bicuspid aortic valve (30% of patients) and aortic coarctation. There are other multiple cardiovascular anomalies, including thoracic aortic aneurysms, which typically involve the ascending aorta.

Many diverse noninfectious and infectious inflammatory aortitis can cause thoracic aortic aneurysms. These conditions include *giant cell arteritis, syphilitic aortitis, mycotic aneurysm (often caused by bacterial endocarditis), Takayasu arteritis, rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, reactive arthritis, Wegener granulomatosis, and Reiter syndrome.* Otherwise, infectious aortitis can occur from a primary bacterial infection of the aortic wall leading to an aneurysm formation. In particular, mycotic aneurysm arise from secondary infections of pre-existing aneurysm, which can result (1) from septic embolization; (2) as a consequence of extension of an adjacent process; or (3) due to circulating microorganisms seeding the damaged aortic wall. Tertiary syphilis is now a rare cause of aortic aneurysms. The bacteria that are most commonly associated with aneurysm formation are *Salmonella* spp., *Staphyllococcus* spp., and *Mycobacterium* spp. HIV is also an infectious agent that can cause aortic aneurysms.

In general, the two most prevalent disorders that predispose to aortic aneurysms are *atherosclerosis* and *hypertension.* Atherosclerosis is the predominant factor in abdominal aortic aneurysms and a significant one for descending thoracic aortic aneurysms, emphasizing the inflammatory nature of aortic aneurysm formation. Hypertension is the most common condition associated with ascending aortic aneurysms. Trauma can also lead to aneurysm formation but, more importantly, it can lead to acute aortic transection and rupture of a pre-existing aortic aneurysm.

Elefteriades JA. Thoracic aortic aneurysm: reading the enemy's playbook. *Curr Prob Cardiol.* 2008;33:203–277.

Guo DC, Papke CL, He R, Milewicz DM. Pathogenesis of thoracic and abdominal aortic aneurysms. *Ann NY Acad Sci.* 2006;1085:339–352.

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Kumar VS, Abbas AK, Fausto J, et al., eds. *Robbins and Cotran Pathologic Basis of Disease.* 8th ed. Philadelphia: Saunders/Elsevier; 2009.

Loeyz BL, Schwarze U, Holm T, et al. Aneurysm syndromes caused by mutations in the TGF-beta receptor. *N Engl J Med.* 2006;335:788–798.

Sievers HH, Schmidtke MD. A classification for the bicuspid aortic valve from 304 surgical specimens. *J Thor Cardiovasc Surg.* 2007;133:1226–1233.

A.3. How are thoracic aortic dissections classified?

Aortic dissections are commonly classified using either the DeBakey or Stanford systems (Fig. 8.4). The DeBakey system classifies aortic dissections by both their site of origin and their distal extension, providing four different categories with potentially distinct clinical implications:

- Type I dissection begins in the ascending aorta and extends throughout the aorta down to the common iliac arteries.
- Type II dissection is limited to the ascending aorta only.

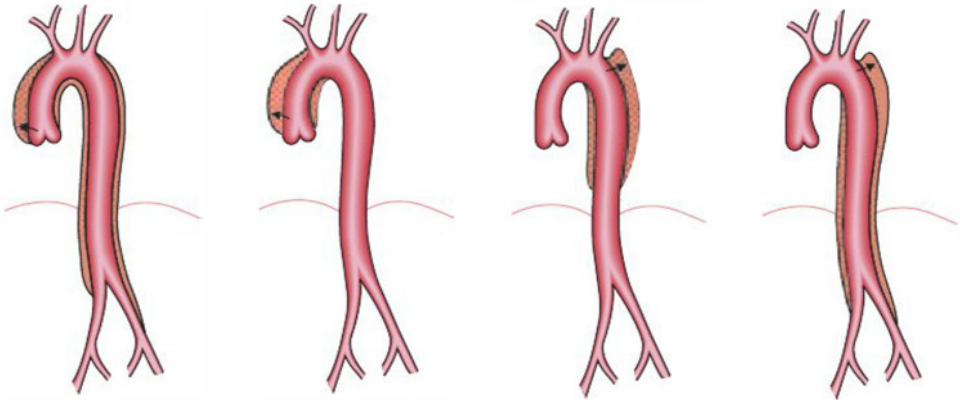

Figure 8.4 Schematic illustration of the Debakey and Stanford systems of classification of aortic dissection. (From Reece T, Green G, Kron I. Aortic dissection. In: Cohn LH, ed. *Cardiac Surgery in the Adult.* New York: McGraw-Hill; 2008:1195–1222, with permission.)

- Type III dissections begin distal to the left subclavian artery and they are subdivided into subtypes a and b depending upon abdominal aortic involvement.
  - Type IIIa dissections end in the descending thoracic aorta.
  - Type IIIb dissections extend into the abdominal aorta.

The Stanford system classifies aortic dissections into types A and B based on the involvement of the ascending aorta only. The Stanford system is a more simple and functional classification based on the premise that the clinical course and surgical significance of aortic dissection is determined by the involvement of the ascending aorta. Some experts argue that patients with type A dissection have different clinical behavior depending on the distal extension.

- Type A dissections affect the ascending aorta regardless of the extension or where the primary tear occurs (Fig. 8.5). This type includes DeBakey's type I and type II dissections.
- Type B dissections originate in the descending aorta and are equivalent to DeBakey's type III dissection (Fig. 8.6A,B).

Beall AC Jr, Lewis JM, Weibel J, et al. Angiographic evaluation of the vascular surgery patient. *Surg Clin North Am.* 1966;46:843–862.

Daily PO, Trueblood H, Stinson E, et al. Management of acute aortic dissections. *Ann Thorac Surg.* 1970;10:237–247.

DeBakey ME, Cooley DA, Crawford ES, et al. Aneurysms of the thoracic aorta. *J Thorac Surg.* 1958;36:393–420.

Reece TB, Green GR, Kron IL. Aortic dissection. In: Cohn LH, ed. *Cardiac Surgery in the Adult*. New York: McGraw-Hill; 2008:1195–1222.

A.4. How are TAAAs classified?

TAAAs compromise the aorta from the origin of the left subclavian artery and can involve variable portions, including extension into the aortic bifurcation. The

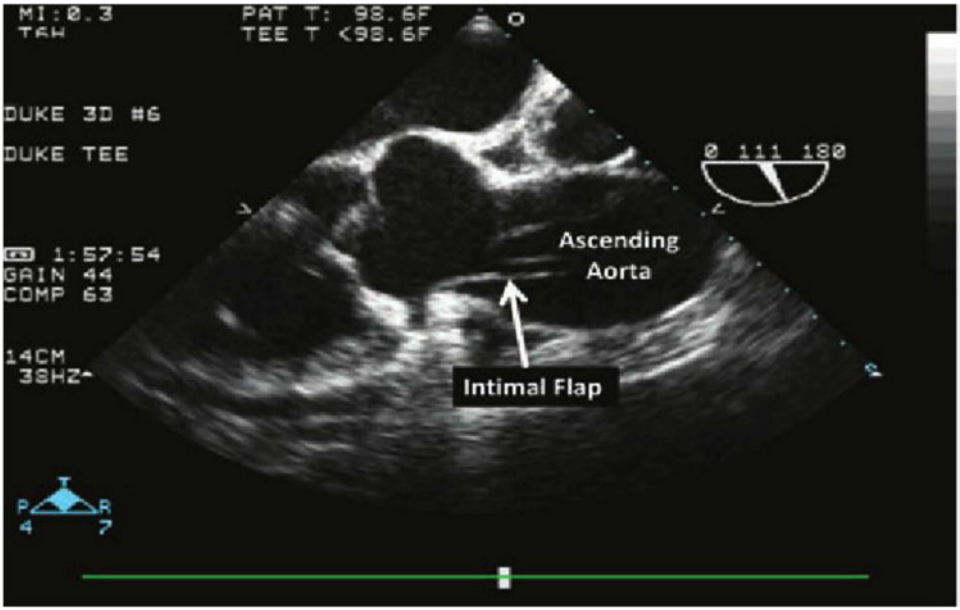

Figure 8.5 Transesophageal echocardiographic image of the ascending aorta demonstrating an intimal flap in the aortic lumen in a patient with a Stanford type A aortic dissection.

Crawford classification system takes into account the extent of aortic involvement, which has significant implications in the selection of treatment and determination of morbidity and mortality associated with surgical repair; but, most importantly, in the assessment of neurologic risk.

There are four Crawford categories (Fig. 8.7) described as follows:

- Type I TAAA originates below the left subclavian artery and extends into the abdominal aorta, including the celiac axis and mesenteric arteries.
- Type II TAAA involves the same areas as type I, but extends caudally to include the infrarenal abdominal aorta.
- Type III TAAA begins in the lower descending thoracic aorta and involves the remainder of the aorta.
- Type IV TAAA begins at the diaphragm and involves the abdominal aorta only.

Coselli JS, LeMaire SA. Descending and thoracoabdominal aortic aneurysms. In: Cohn LH, ed. *Cardiac Surgery in the Adult*. New York: McGraw-Hill; 2008:1277–1298.

Crawford ES, Crawford JL, Safi HJ, et al. Thoracoabdominal aneurysms: preoperative and intraoperative factors determining immediate and long-term results in 605 patients. *J Vasc Surg*. 1986;3:389–404.

A.5. Describe the natural history and clinical presentation of TAAAs.

Thoracic aortic aneurysms grow at a very slow rate (average 0.12 cm per year). The rate of growth is greater for descending (0.3 cm per year) versus ascending aorta aneurysms (0.1 cm per year). Aortic aneurysms grow at a faster rate when there has been a chronic dissection of a pre-existing aneurysm or in patients with Marfan

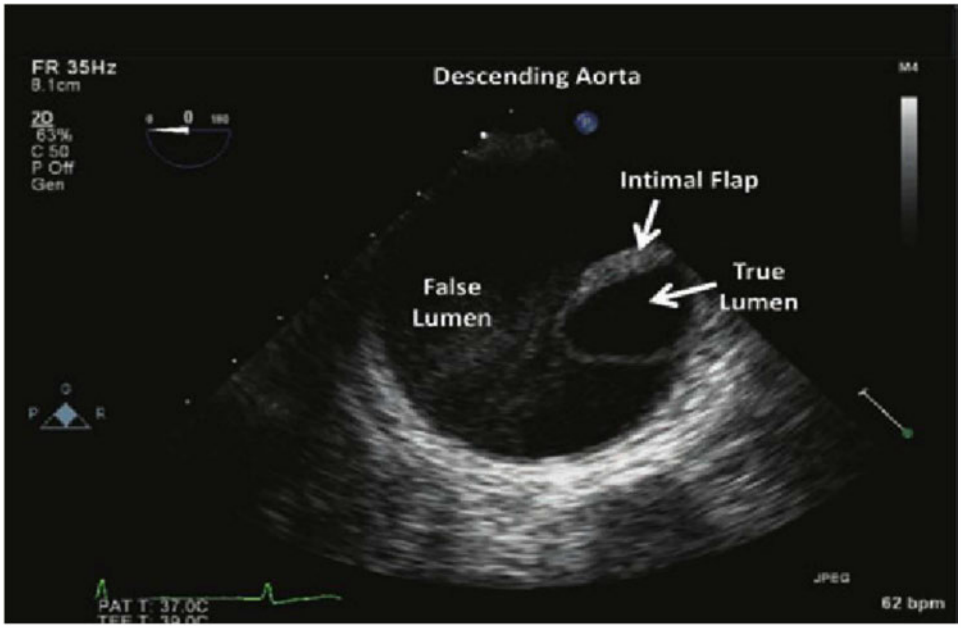

Figure 8.6 Transesophageal echocardiographic image of the descending thoracic aorta in a patient with a Stanford type B aortic dissection demonstrating the true and false lumens separated by an intimal flap. Panel **A** shows the aorta in short axis, while panel **B** shows a long axis view in the same patient.

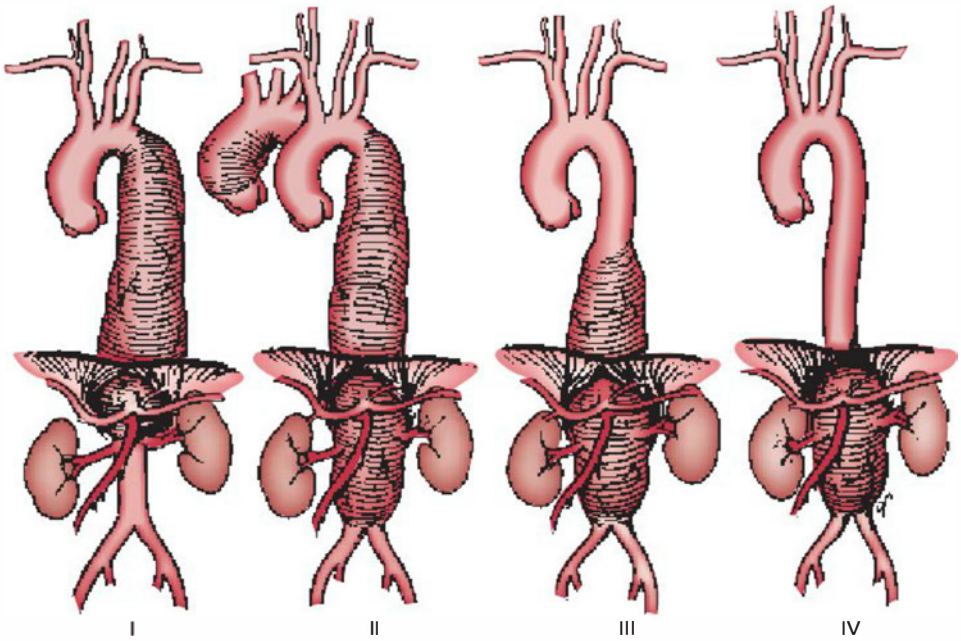

Figure 8.7 Schematic illustration of the Crawford system of classification of thoracoabdominal aortic aneurysms. (From Coselli J, LeMaire S. Descending and thoracoabdominal aortic aneurysms. In: Cohn LH, ed. *Cardiac Surgery in the Adult*. New York: McGraw-Hill; 2008:1277–1298, with permission.)

syndrome. Most commonly, TAAAs grow in an asymptomatic fashion (~43% of patients) until diagnosis is made incidentally when an imaging study is obtained for an unrelated reason. Only 5% to 10% of patients present with symptoms. Aneurysms can produce pain from aortic wall stretching or extrinsic compression of contiguous structures depending upon their location. Ascending aortic aneurysms can produce retrosternal pain, whereas descending ones can cause interscapular pain. Chest wall or posterior chest pain may arise from compression or erosion of ribs and vertebral bodies, respectively. Associated symptoms such as cough and dyspnea, caused by tracheal or airway impingement, are more common in ascending and arch aneurysms. Hemoptysis can occur from erosion of TAAAs into bronchi or lung parenchyma. There may be hoarseness or dysphagia from compression of the recurrent laryngeal nerve or the esophagus, respectively. TAAAs can be a source of atheroembolism to peripheral tissues due to mural thrombosis. Otherwise, in many instances, the presenting feature is rupture or dissection, leading to death. It is critical to have a high index of suspicion whenever a patient has chest pain of unknown cause.

The incidence of TAAAs is 10 per 100,000 patient-years, and is similar among women and men. The fact that the mid- to long-term survival of patients with aneurysms is poor (5-year survival rate of 19.2%), and the main cause of death in these patients is aneurysm rupture (51%) emphasizes the importance of early diagnosis and management. The major complications of thoracic aneurysms are rupture and dissection, which occur at a rate of 7% per year. The incidence of rupture, dissection, or death increases in a linear fashion as the aorta grows, reaching maximal levels at an aortic diameter of 6 cm, beyond which the aorta reaches the limits of its mechanical

properties and distensibility, and the rate of complications increases exponentially. Indeed, the lifetime risk of rupture or dissection above this point is 34%. Therefore, the diagnosis before this "hinge-point" at which the rate of rupture, dissection, and death increases at an unacceptable level is crucial. In general, it is accepted that intervention should occur when the annual risk of rupture and/or dissection exceeds the risk for surgical repair. Other factors, such as patient age, comorbidities, aneurysm morphology and extent, as well as surgical expertise, are important considerations for decision-making purposes.

There are certain patient-related predictors of rupture. Advanced age increases the relative risk of thoracic aortic disruption by a factor of 2.6 for every decade of life. The presence of chronic obstructive pulmonary disease (COPD) is another significant predictor of rupture. Patients with TAAAs and chest or back pain are also at increased risk of aneurysm rupture. In several studies, women have had both faster rates of aneurysm expansion and higher rate of aneurysm rupture (approximately 79% of ruptures occur in women). Hypertension and obstructive sleep apnea, although correlating with aneurysm development, have not conclusively shown to increase the risk of rupture.

Dapunt OE, Galla JD, Sadeghi AM, et al. The natural history of thoracic aortic aneurysms. *J Thorac Cardiovasc Surg*. 1994;107:1323–1333.

Davies RR, Goldstein LJ, Coady MA, et al. Yearly rupture or dissection rates for thoracic aortic aneurysms: simple prediction based on size. *Ann Thorac Surg*. 2002;73:17–28.

Elefteriades JA. Thoracic aortic aneurysm: reading the enemy's playbook. *Curr Prob Cardiol*. 2008;33:203–277.

Elefteriades JA, Farkas EA. Thoracic aortic aneurysm: clinically pertinent controversies and uncertainties. *J Am Coll Cardiol*. 2010;55:841–857.

Gleason TG, Benjamin LC. Conventional open repair of descending thoracic aortic aneurysms. *Perspect Vasc Surg Endovasc Ther*. 2007;19:110–121.

Griepp RB, Ergin MA, Galla JD, et al. Natural history of descending thoracic and thoracoabdominal aneurysms. *Ann Thorac Surg*. 1999;67:1927–1930.

Ince H, Nienaber CA. Etiology, pathogenesis and management of thoracic aortic aneurysm. *Nat Clin Pract Cardiovasc Med*. 2007;4:418–427.

Juvonen T, Ergin MA, Galla JD, et al. Prospective study of the natural history of thoracic aortic aneurysms. *Ann Thorac Surg*. 1997;63:1533–1544.

Mason RH, Ruegg G, Perkins J, et al. Obstructive sleep apnea in patients with abdominal aortic aneurysms: highly prevalent and associated with aneurysm expansion. *Am J Respir Crit Care Med*. 2011;183:668–674.

Mofidi R, Goldie VJ, Kelman J, et al. Influence of sex on expansion rate of abdominal aortic aneurysms. *Br J Surg*. 2007;94:310–314.

A.6. What are the indications for and timing of surgical intervention for TAAAs? Describe the medical management.

Both the etiology and location of an aneurysm may affect its growth rate and propensity for dissection or rupture. The main determinants of the risk of rupture or dissection for TAAAs are size and rate of expansion. As such, surgical intervention is performed when the aneurysm is large enough to be considered at significant risk for rupture. The initial size is an important predictor of the rate of aneurysm growth. In this regard, the annual rate of rupture or dissection is 2% for aneurysms less than 5 cm, 3% for aneurysms 5 to 5.9 cm, and 7% for aneurysms 6 cm or more in diameter.

Medical therapy to slow aneurysm growth or to reduce the risk of dissection or rupture has met with limited success. Long-term β-blocker therapy has been shown to significantly slow the rate of aortic dilatation and to lower mortality. Recently,

oral losartan has shown promise in decreasing aneurysmal degeneration rate in murine models of Marfan syndrome. This data is the precedent for the ongoing COMARE study (COzaar in Marfan pAtients Reduces aortic Enlargement). The goal of antihypertensive therapy is to maintain systolic blood pressure (BP) between 105 and 120 mm Hg. Patients should be followed with serial imaging studies for surveillance. A second imaging study should be obtained 6 months after initial diagnosis. If the aneurysm is unchanged in size, it is then reasonable to obtain an imaging study annually in most cases, except patients with Marfan syndrome or acute aortitis. Should there be a significant increase in aneurysm size between studies, the study interval should be decreased to 3 or 6 months. The optimal timing of surgical repair of thoracic aortic aneurysms depends both on the aneurysm size, patient size, degree of aortic valvular pathology, rate of aneurysm growth, and the patient's associated comorbidities. As previously mentioned, the goal of aortic aneurysm surgery is to prevent aortic rupture or dissection. Therefore, for ascending thoracic aortic aneurysms in patients without significant comorbidities, surgery is indicated at an aortic diameter of 5.5 cm or greater. The threshold for surgery is raised to 6 cm or more for patients with an increased operative risk (e.g., the elderly or those with comorbidities). The threshold is lowered to 5 cm if a patient has a bicuspid aortic valve as those patients are at risk for aortic rupture or dissection at a smaller aortic diameter. In patients with collagen vascular diseases such as Marfan syndrome or Loeys-Dietz, aortic repair is recommended at 4 cm. Indeed, when patients with a bicuspid aortic valve require valve replacement surgery, the recommendation is for prophylactic replacement of the ascending aorta if its diameter is 4.5 cm or more. Patient size can also play a role in the decision to operate on an aortic aneurysm. It is appropriate to use an aortic size index, especially in very small or very large individuals. Rate of growth of an aortic aneurysm can also be an indication for aortic repair. Although this is usually caused by inaccurate imaging measurements, a rate of growth greater than 1.0 cm per year can be an indication for surgery. This scenario is usually seen in patients with prior aortic dissection. Given the increased operative risk in descending thoracic aneurysms, surgery is recommended at an aortic diameter of 6 cm or more.

Davies RR, Goldstein LJ, Coady MA, et al. Yearly rupture or dissection rates for thoracic aortic aneurysms: simple prediction based on size. *Ann Thorac Surg*. 2002;73:17–28.

Devereux RB, Roman MJ. Aortic disease in Marfan's syndrome. *N Engl J Med*. 1999; 340:1358–1359.

Elefteriades JA, Botta DM. Indications for the treatment of thoracic aortic aneurysms. *Surg Clin N Amer*. 2009;89:845–867.

Isselbacher EM. Thoracic and abdominal aortic aneurysms. *Circulation*. 2005;111:816.

B. Preoperative Evaluation and Preparation

B.1. How should TAAAs be surgically evaluated?

Preoperative assessment of the patient for elective TAAA repair requires a delicate balance between the risks of aneurysm rupture versus surgical morbidity. The mortality of TAAA repair may range from 3% to 23%. Particularly, the incidence of spinal cord injury is 3% to 18%, with long-term survival being shorter in patients who suffer postoperative paraplegia or paraparesis. Indeed, the 5-year survival rate for patients with spinal cord injury was 44%, whereas it was 62% for those without spinal cord injury. Therefore, the determination of neurologic risk and anatomic planning of the procedure is crucial to minimize complications. Moreover, the incidence of spinal cord injury is related with the complexity of the repair and the possible need and duration of aortic cross-clamping.

Once the decision has been made to proceed with surgical repair, a comprehensive radiographic evaluation of the aorta is necessary for operative planning. Due to the advanced capabilities of modern helical computed tomography (CT), a high-quality CT angiogram is usually sufficient (Fig. 8.8). Contrast arteriography or magnetic resonance angiography is rarely required. All iodinated contrast studies should be performed well in advance of the planned procedure to avoid contrast-related acute kidney injury (AKI). Patients with baseline renal insufficiency may receive *N*-acetylcysteine and intravenous hydration to reduce the risk of contrast-induced nephropathy and postoperative AKI. Preoperative assessment of the aneurysm anatomy and of the major branches is critical to surgical planning. Open TAAA repair can be performed with or without distal aortic perfusion as well as with cardiopulmonary bypass (CPB) with or without deep hypothermic circulatory arrest (DHCA). Determinants of this decision include aneurysm and aortic anatomy, patient body habitus, the expected difficulty of aortic exposure, and the expected risk of postoperative end-organ dysfunction. Recent studies have demonstrated preserved end-organ function and decreased paraplegia utilizing CPB with DHCA. Endovascular repair of



Figure 8.8 Three-dimensional reconstruction CT angiogram of a large transverse arch aneurysm extending to within a centimeter of the left common carotid artery, but with ≥ 2 cm of proximal landing zone distal to the innominate artery. (From Hughes GC, Sulzer CF, McCann RL, Swaminathan M. Endovascular approaches to complex thoracic aortic disease. *Semin Cardiothorac Vasc Anesth.* 2008;12:298–319, with permission.)

TAAAs does not require CPB or distal aortic perfusion, as the duration of aortic flow disruption is quite limited.

Unfortunately, the studies used to assess the aneurysm vasculature are imperfect with respect to delineating the spinal cord blood supply. CT angiography and magnetic resonance angiography detect the artery of Adamkiewicz in only 50% to 80% of patients. This is significant as the risk of postoperative paraplegia is 5% if the artery of Adamkiewicz is identified preoperatively and reimplanted, whereas it is as high as 50% if the artery is not identified and reattached.

Davies RR, Goldstein LJ, Coady MA, et al. Yearly rupture or dissection rates for thoracic aortic aneurysms: simple prediction based on size. *Ann Thorac Surg*. 2002;73:17–27; discussion 27–28.

Fehrenbacher JW, Hart DW, Huddleston E, et al. Optimal end-organ protection for thoracic and thoracoabdominal aortic aneurysm repair using deep hypothermic circulatory arrest. *Ann Thorac Surg*. 2007;83:1041–1046.

Kieffer E, Ricard T, Chiras J, et al. Preoperative spinal cord arteriography in aneurysmal disease of the descending thoracic and thoracoabdominal aorta: preliminary results in 45 patients. *Ann Vasc Surg*. 1987;3:34–46.

Levine WC, Lee JJ, Black JH, et al. Thoracoabdominal aneurysm repair: anesthetic management. *Int Anesth Clin*. 2005;43:39–60.

Radonic T, de Witte P, Baars MJ, et al. Losartan therapy in adults with Marfan syndrome: study protocol of the multi-center randomized controlled COMPARE trial. *Trials*. 2010;11:3.

Svensson LG, Crawford ES, Hess KR, et al. Experience with 1509 patients undergoing thoracoabdominal aortic operations. *J Vasc Surg*. 1993;17:357–370.

Tabayashi K. Spinal cord protection during thoracoabdominal aneurysm repair. *Surg Today*. 2005;35:1–6.

B.2. Describe the preoperative evaluation and risk assessment of the patient scheduled for TAAA repair.

The preoperative evaluation of a patient undergoing TAAA repair requires a thorough multisystem assessment. The goal is to diagnose comorbidities, assess the risk of adverse outcomes, optimize medical status, and plan an anesthetic technique that reduces the risk of complications. Cardiovascular diseases, including hypertension (70% to 90% of patients) and coronary artery disease (CAD) (50% of patients), are common. Accurate assessment of baseline cardiac function is mandatory for perioperative decision making. All patients should undergo pharmacologic stress/nuclear perfusion tests to evaluate myocardial ischemic risk and, if there is evidence of heart failure, there should be a complete assessment of valvular and ventricular function. Angioplasty or coronary artery bypass graft surgery should be considered in patients with significant CAD. Cerebrovascular disease and symptomatic lower extremity arterial occlusive disease occur in 15% of patients. The risk of perioperative cardiac morbidity and mortality is approximately 12% to 15%.

History of smoking and significant COPD is common in this population. About 25% of patients have significant COPD as manifested by a forced expiratory volume in 1 second below 50%. Although impairment in pulmonary function can be detected on a clinical basis, pulmonary function tests add useful prognostic information, as COPD is a significant risk factor. In fact, postoperative respiratory failure is a major complication (25% to 45% of cases) and a leading cause of mortality in patients undergoing TAAA repair. Moreover, pulmonary function tests are instrumental for planning purposes as one-lung ventilation is essential for surgical repair of type I, II, and III aneurysms. Patients with poor diffusing capacity or severe COPD may require the use of CPB for TAAA repair, as they may not be able to tolerate one-lung ventilation. As a

large aneurysm can distort the left mainstem bronchus, CT scan may give vital information relevant to double lumen endotracheal tube placement.

Associated visceral and renovascular disease is reported in about 30% of patients. Among surgical candidates for TAAA repair, 13% to 24% have baseline chronic kidney disease (CKD) (serum creatinine >1.5 mg per dL). A significantly increased creatinine level (>1.8 mg per dL) is present in 15% of patients. In cases with extensive visceral compromise and aneurysmal occlusion of more than one visceral/renal artery, a creatinine level >2.5 mg per dL is a relative contraindication to elective surgery unless there is evidence of potential renal function preservation or recovery with renal artery reconstruction. Preoperative CKD is associated with an increased risk of postoperative AKI and up to an eightfold increase in perioperative mortality.

The contemporary operative mortality for TAAA repair ranges from 7% to 10%, with higher volume surgeons having the best results in centers of reference. Of special note, surgical treatment in nonelective situations doubles both perioperative mortality and the incidence of complications. Another predictor of poor outcome is advanced age or, more importantly, decreased overall functional status. In general, the presence of more comorbidities increases the perioperative risk. Otherwise, as mentioned above, patients who sustain major neurologic deficits have a significantly increased risk of operative mortality. Paraplegia and stroke rates range from 1.5% to 5% and 1.3% to 7.5%, respectively. Five-year survival rates are about 65% with mid- and long-term mortality usually unrelated to the surgical intervention.

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Cambria RP, Clouse WD, Davison JK, et al. Thoracoabdominal aneurysm repair: results with 337 operations performed over a 15-year interval. *Ann Surg*. 2002;236:471–479.

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Gleason TG, Benjamin LC. Conventional open repair of descending thoracic aortic aneurysms. *Perspect Vasc Surg Endovasc Ther*. 2007;19:110–121.

Kahn RA, Stone ME, Moskowitz DM. Anesthetic consideration for descending aortic neurysm repair. *Sem Cardiothorac Vasc Anesth*. 2007;11:205–223.

Kouchoukos NT, Dougenis D. Surgery of the thoracic aorta. *N Engl J Med*. 1997;336:1876–1889.

Levine WC, Lee JJ, Black JH, et al. Thoracoabdominal aneurysm repair: anesthetic management. *Int Anesth Clin*. 2005;43:39–60.

Svensson LG, Crawford ES, Hess KR, et al. Experience with 1509 patients undergoing thoracoabdominal aortic operations. *J Vasc Surg*. 1993;17:357–368.

Svensson LG, Hess KR, Coselli JS, et al. A prospective study of respiratory failure after high-risk surgery on the thoracoabdominal aorta. *J Vasc Surg*. 1991;14:271–282.

B.3. Describe the spinal cord blood supply.

The spinal cord has a system of longitudinal and transverse arteries. The most important longitudinal arteries are a single anterior spinal artery supplying 75% of the cord and a pair of posterior spinal arteries supplying the remaining 25%. The anterior spinal artery is unique, because it is a single long vessel supplying the anterior portion of the spinal cord that principally controls motor function. Also, the anterior spinal artery receives minimal contribution from transverse radicular arteries, which result in little blood flow reserve to the anterior spinal cord. The territory supplied by the anterior spinal artery is divided into three functionally distinct levels: cervicodorsal, midthoracic, and thoracolumbar. The cervicodorsal region receives its blood supply from the vertebral, subclavian, thyrocervical, and costocervical arteries. The

midthoracic region is supplied only by a left or right intercostal artery arising between the fourth and the ninth thoracic vertebrae. The thoracolumbar region of the anterior spinal artery receives its blood supply mainly from one of the intercostal arteries called the *arteria radicularis magna* (ARM) or the artery of Adamkiewicz. It arises at the level of T5–T8 in 15%, T9–T12 in 60%, L1 in 14%, and L2 in 10% of patients. If the aortic cross-clamp is applied distal to the ARM, there is low probability of spinal cord ischemic injury. Otherwise, if this artery is patent and arises from the aneurysm wall or distal to the level of the cross-clamp, a significant risk of spinal cord injury is incurred. The anterior spinal artery is smaller above than below the entry of the ARM. Resistance to blood flow is 51 times greater going "up" the anterior spinal artery. Therefore, distal aortic perfusion during thoracic aortic cross-clamping protects the spinal cord below the ARM, but has minimal impact above it. The distal spinal cord and cauda equina are supplied by the hypogastric arteries in the pelvis.

Recently, multiple anastomotic pathways outside the spinal canal, in the perivertebral tissues and in the paraspinous muscles that connect to each other and to the spinal cord arteries, have been described. According to this "collateral network" concept, there can be increased blood flow from any one of these sources if the flow to another is reduced. In a similar fashion, a steal phenomenon can occur if an alternate pathway of low resistance is available. Evidence of this phenomenon comes from the clinical observation of back bleeding from intercostal arteries into an open aortic segment after exclusion by cross-clamping during surgical repair.

Black JH, Cambria RP. Contemporary results of open surgical repair of descending thoracic aortic aneurysms. *Sem Vasc Surg.* 2006;19:11–17.

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DiChiro G, Fried LC, Doppman JL. Experimental spinal angiography. *Br J Radiol.* 1970;43:19–30.

Griepp RB, Griepp EB. Spinal cord perfusion and protection during descending thoracic and thoracoabdominal aortic surgery: the collateral network concept. *Ann Thorac Surg.* 2007; 83:S865–S869.

Kahn RA, Stone ME, Moskowitz DM. Anesthetic consideration for descending aortic aneurysm repair. *Sem Cardiothorac Vasc Anesth.* 2007;11:205–223.

Piccone W, DeLaria GA, Najafi H. Descending thoracic aneurysms. In: Bergan JJ, Yao JST, eds. *Aortic Surgery*. Philadelphia: WB Saunders; 1989:249.

Svensson LG, Richards E, Coull A, et al. Relationship of spinal cord blood flow to vascular anatomy during thoracic aortic cross-clamping and shunting. *J Thorac Cardiovasc Surg.* 1986;91:71–78.

C. Intraoperative Management

C.1. What hemodynamic monitors should be used for the patient undergoing TAAA repair?

Initially, all patients should have standard American Society of Anesthesiologists monitors applied. Particularly, multilead ECG with ST-segment analysis is essential as the incidence of intraoperative myocardial ischemia and arrhythmias is significant. Given the extensive and anticipated hemodynamic changes, a direct continuous invasive monitoring of arterial BP is mandatory. In this regard, right radial artery is the preferred site because it reflects pressure in the carotid arteries. If the aneurysm extends proximally, requiring surgical manipulation close to the aortic arch, monitoring of the left radial pressure can be helpful for assessment of left subclavian artery patency. In this situation, the proximal application of the aortic cross-clamp may disrupt left subclavian arterial blood flow, rendering left radial monitoring useless. Otherwise, monitoring of

femoral arterial pressure allows assessment of perfusion distal to the aortic cross-clamp during partial left heart bypass. It is also instrumental in evaluating the adequacy of surgical repair by documenting the simultaneous pressure gradient between upper and lower body (across the repair). The femoral vessels should be accessed in consultation with the surgeon given the possibility of extracorporeal circulation or placement of an intra-aortic balloon pump. Placement of a pulmonary artery catheter should be strongly considered in order to assess preload and afterload as well as to monitor for perioperative left ventricular dysfunction and ischemia.

The use of transesophageal echocardiography (TEE) during TAAA repair allows confirmation of the extent and severity of the aortic disease. It also gives real-time functional and hemodynamic information regarding biventricular and valvular compromise. Ventricular dysfunction and regional wall motion abnormalities can be readily diagnosed. TEE can also assist during the placement of perfusion cannulae and offers valuable information at a low risk of complications. Of note, because of the lateral positioning of the patient, presence of the TEE probe may cause "pressure" injury of both tissues and neurovascular structures in the posterior larynx (recurrent laryngeal nerve, vocal cords, etc.). Thus, the risk and benefit of TEE monitoring must be weighed carefully. Theoretically, a pediatric probe may lessen the aforementioned complications.

Large-bore intravenous access is essential for TAAA repair, as the potential for rapid intraoperative blood loss is significant. One or two large-bore peripheral intravenous catheters are recommended along with a large-bore central venous introducer. Left upper extremity peripheral intravenous catheters should be avoided during aortic arch surgery, because the left innominate vein may be injured or intentionally ligated during the procedure. Central venous access allows monitoring of cardiac filling pressures, and also permits infusion of medications, intravenous fluids, and blood products. The femoral vein can be accessed with a large-bore introducer to permit rapid infusion of fluids or blood products to the lower body, which can be useful during distal perfusion or partial left-heart bypass (LHB). Once again, a preoperative discussion with the surgical team is highly desirable for formulating a coherent strategy. The use of rapid infusing systems with a heat exchanger for delivery of high volume of intravenous fluids and blood products is considered standard. Besides invasive direct hemodynamic monitoring, placement of a urinary catheter is mandatory in order to assess fluid balance/urinary output and renal perfusion.

Coselli JS, LeMaire SA. Tips for successful outcomes for descending thoracic and thoracoabdominal aortic aneurysm procedures. *Sem Vasc Surg*. 2008;21:13–20.

Kahn RA, Stone ME, Moskowitz DM. Anesthetic consideration for descending aortic aneurysm repair. *Sem Cardiothorac Vasc Anesth*. 2007;11:205–223.

Levine WC, Lee JJ, Black JH, et al. Thoracoabdominal aneurysm repair: anesthetic management. *Int Anesth Clin*. 2005;43:39–60.

C.2. What are the possible blood conservation techniques and blood product requirements for TAAA repair?

TAAA repair is associated with the potential for massive blood loss. The anticipated requirements for blood products may exceed several blood volumes in extreme circumstances. As such, intraoperative and postoperative coagulopathy are common. The causes of coagulopathy are hemodilution and massive transfusion, platelet dysfunction, heparin effects, and fibrinolysis. The most common defects include quantitative and qualitative platelet dysfunction attributable to hypothermia and the use of extracorporeal circulation. Apparently, the event that initiates fibrinolysis is visceral ischemia due to supraceliac aortic cross-clamping. Acute peripheral ischemia (other than mesenteric) also enhances the fibrinolytic state by promoting activity of tissue-type plasminogen activator and a decrease in plasminogen activator inhibitor.

Although the use of antifibrinolytic agents should be considered during the perioperative period in order to minimize blood loss, several studies have suggested that antifibrinolytic therapy is of limited efficacy in the setting of TAAA repair. Therefore, blood salvaging techniques for autotransfusion are essential. The use of a device for centrifugation after collection and washout out of red cells ("cell saver") is the most commonly used technique. Unfortunately, the use of "cell saver" induces loss of platelets, plasma proteins, and coagulation factors. There is also a time delay associated with processing of the shed blood. Otherwise, in heparinized patients, the use of a cardiotomy suction/reservoir permits the autotransfusion of filtered unwashed whole blood, which has significant advantages due to the preservation of platelets and coagulation factors. Some institutions advocate collection of autologous blood by acute normovolemic hemodilution performed in selected patients usually before or soon after anesthetic induction. Early communication with the blood bank is imperative to ensure that adequate quantities of packed red blood cells (pRBCs), fresh frozen plasma, platelets, and, possibly, cryoprecipitates are available. Five to ten units of pRBCs should be immediately available in the operating room, with a similar number of units available in the blood bank. A similar amount of fresh frozen plasmas, typically in a ratio of one per two or three pRBCs transfused should be readily available in order to avoid further dilution of clotting factors.

The use of moderate heparinization before aortic cross-clamping prevents the initiation of the clotting cascade and reduces the incidence of disseminated intravascular coagulation. Unlike full CPB, a reduced dose of heparin may be used for partial bypass. The potential complications of this approach are bleeding and coagulopathy. Additionally, if heparin is used as an anticoagulant in the cell saver, additional protamine sulfate may need to be administered.

Coselli JS, LeMaire SA. Tips for successful outcomes for descending thoracic and thoracoabdominal aortic aneurysm procedures. *Sem Vasc Surg*. 2008;21:13–20.

Kahn RA, Stone ME, Moskowitz DM. Anesthetic consideration for descending aortic aneurysm repair. *Sem Cardiothorac Vasc Anesth*. 2007;11(3):205–223.

Levine WC, Lee JJ, Black JH, et al. Thoracoabdominal aneurysm repair: anesthetic management. *Int Anesth Clin*. 2005;43:39–60.

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C.3. Describe the surgical approach to TAAA repair.

- *Position*. The surgical approach is typically through the left chest, with the patient in a partial right lateral decubitus position and the hips almost supine to allow femoral cannulation, if necessary.
- *Incision*. The incision is tailored to complement the extent of the aneurysm. For Crawford types II, III, or IV aneurysms, a thoracoabdominal incision is made from the symphysis pubis, extending midline to the umbilicus, curving straight into the costal cartilage and into a posterolateral thoracotomy incision. For types I and IV, a modified thoracoabdominal incision is used, where the incision extends from the umbilicus to the chest and exposes the upper abdominal aorta. In this manner, an aortic cross-clamp can be applied either above or below the renal arteries. In either case, the intra-abdominal portion of the dissection is performed in the retroperitoneal space after the diaphragm is divided.
- *Cannulation for left-heart bypass (LHB)*. Left atrial-to-femoral artery bypass is often used in patients with significant myocardial dysfunction or other systemic disease and in patients with extensive aneurysms that would require prolonged

aortic cross-clamping. Typically, an outflow cannula is placed in the left atrium, and blood is routed through a centrifugal pump to an inflow cannula in the right femoral artery. Unlike CPB, the use of LHB requires reduced heparinization (100 U per kg of heparin approximately 5 minutes before cannulation). The potential advantage of LHB includes improved perfusion of the lower extremities and possibly of the anterior spinal artery through collateral vessels, while the proximal aorta is cross-clamped. The use of LHB therefore minimizes the development of acidosis in the lower extremities, which, in turn, improves hemodynamic stability upon release of the aortic cross-clamp. LHB is typically initiated at a rate of 500 mL per minute, and once the proximal aortic clamp is placed, the flows are adjusted to maintain the proximal aortic pressure above 90 mm Hg or distal mean arterial pressure of approximately 70 mm Hg.

- *Cannulation for CPB with DHCA*. The use of CPB with DHCA obviates the need for proximal aortic cross-clamping and potential spinal cord injury. In some institutions, this is the preferred method for all open repairs. Studies have shown preserved end-organ function (especially renal) as well as decreased paraplegia when a DHCA strategy is utilized. A thorough TEE evaluation is necessary prior to surgery, as this approach is contraindicated in patients with more than mild aortic valve insufficiency as the heart can significantly distend when fibrillation occurs with cooling. Typically, a right femoral venous cannula is placed via either an open approach, or percutaneously using the Seldinger technique prior to positioning the patient in the partial right lateral decubitus position. The venous cannula is advanced into the right atrium using TEE or fluoroscopy for guidance. Arterial cannulation can be obtained at the distal arch, proximal descending aorta, axillary artery, or femoral artery depending on the anatomy of the aneurysm and the planned repair. The pericardium is opened and a left ventricular vent is placed via the left ventricular apex or the left inferior pulmonary vein. During the circulatory arrest, some strategies utilize antegrade cerebral perfusion, direct cannulation and antegrade perfusion of visceral segments, or a combination of the two.
- *Proximal aortic anastomosis*. In type I and II repairs, the proximal thoracic aorta distal to the left subclavian is dissected away from the esophagus in order to prevent a possible esophageal–aortic fistula. Following circulatory arrest (or the placement of proximal aortic cross-clamp if LHB is utilized), an appropriately sized Dacron graft is then sutured proximally to the descending thoracic aorta and checked for hemostasis. Once the proximal anastomosis is completed, the descending aortic graft is cannulated and CPB reinitiated. With each subsequent anastomosis, the clamp can be moved further distally on the graft, sequentially reperfusing visceral segments.

When utilizing the LHB strategy, the aneurysm is opened. The celiac axis, superior mesenteric artery (SMA), and renal arteries are then identified and perfused with special catheters in order to protect the mesentery. The catheters perfusing the kidneys are typically passed through an ice-bath, maintaining the renal artery temperature below 15°C (59°F). Where feasible, reattachment of patent segmental intercostal and lumbar arteries in the T8 to L1 region is then performed. Intercostal arteries in the T4–T8 region are usually ligated if they exhibit excessive retrograde bleeding, indicating good collateral circulation. If the intercostal arteries between T8 and L1 are occluded by intimal atherosclerosis, patent intercostal arteries in the T4–T8 region may be reattached to preserve circulation.

- *Visceral aortic anastomoses*. The visceral aortic anastomoses are evaluated intraoperatively. It is important to avoid a single patch technique to re-implant visceral artery segments, especially in patients with collagen vascular diseases. Therefore, one may employ a specially manufactured multiple branch Dacron graft to anastomose each visceral artery segment individually in an end-to-end manner. This avoids the long-term complications of visceral patch aneurysms seen in many patients with prior TAAA repair. Once the anastomoses are complete, visceral

perfusion is stopped and the cannulas removed. The patient is then placed in a head-down position, the aortic graft flushed proximally, and then the aortic cross-clamp slowly released. The clamp is then moved to the abdominal aortic graft from distal to visceral anastomoses.

- *Distal aortic anastomosis*. The graft is now cut to the appropriate length and is sutured to the infrarenal aorta. Before the completion of the distal anastomosis, the graft is flushed proximally and the aorta distally. The lower clamp is slowly released to restore the pulsatile flow to the viscera. Large patent lumbar arteries can be re-implanted on the graft and smaller lumbar arteries can be ligated.
- *Other techniques*. The "clamp and sew" technique involves clamping the proximal descending thoracic aorta and replacing the aneurysm with a graft. The distal anastomosis to the lower abdominal aorta is then performed without a clamp, allowing the distal aorta to decompress. Although this technique avoids the need for full heparinization, it imposes a time limit on the surgeon as there is no pump to support distal or collateral perfusion.

Coselli JS, LeMaire SA. Left heart bypass reduces paraplegia rates after thoracoabdominal aortic aneurysm repair. *Ann Thorac Surg*. 1999;67:1931–1934.

Coselli JS, LeMaire SA, Figueiredo LP, et al. Paraplegia after thoracoabdominal aortic aneurysm repair: is dissection a risk factor? *Ann Thorac Surg*. 1997;63:28–36.

Fehrenbacher JW, Hart DW, Huddleston E, et al. Optimal end-organ protection for thoracic and thoracoabdominal aortic aneurysm repair using deep hypothermic circulatory arrest. *Ann Thorac Surg*. 2007;83:1041–1046.

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C.4. What are the specific considerations for anesthetic management of the patient for TAAA repair?

In general, patients with TAAAs have multisystem organ involvement due to the presence of generalized atherosclerosis and other coexisting medical conditions. Initially, the objective is to perform a pre-anesthetic evaluation that detects such comorbidities and assesses the perioperative risks while optimizing the patient's medical status. A careful anesthetic plan should devise a technique that minimizes complications. There should be a clear understanding that this patient population remains at high-risk even with optimal preoperative management given the nature of TAAAs and the surgical procedure (intrathoracic, aortic, and major vascular). Moreover, many patients present on an emergent basis, which precludes ideal preoperative evaluation and optimization, and, in turn, increases the risks for complications.

All antihypertensive and antianginal medications should be continued during the preoperative period to decrease the possibility of myocardial ischemia and aneurysm leakage. Judicious sedation and pain control will offer a similar benefit but clinical signs of complications or neurologic deterioration and organ ischemia (e.g., abdominal pain) can be missed if there is obtundation. Other conditions such as airway protection and risk of aspiration should also be taken into consideration. Importantly, patients can present with established hemodynamic instability and organ malperfusion due to hemorrhage, pericardial tamponade, myocardial ischemia, congestive heart failure, and renal failure.

In addition to extensive hemodynamic monitoring (already discussed) and placement of a urinary catheter, monitoring of differential temperature between central (bladder or rectal) and core (blood or esophageal) compartments is essential. A tympanic or nasopharyngeal probe will approximate brain temperature. A double-lumen endotracheal tube for one-lung ventilation provides optimal surgical exposure,

potentially decreases the injury to the lung by avoiding additional manipulation, and protects the contralateral lung from contamination by blood or other secretions. The method for one-lung isolation varies from one practitioner to another, each providing strong support for his or her preference. Critically important is the ability to provide single-lung ventilation and preparedness to troubleshoot problems as they arise. If placement of a double-lumen tube poses significant risk of aneurysm injury or if there is evident left main bronchus distortion, lung isolation with a bronchial blocker may be a safer alternative. At the end of the surgical procedure, significant airway edema may preclude the exchange of a double-lumen for a single-lumen endotracheal tube.

The main goal of the anesthetic management is to avoid hemodynamic changes that will increase the risk of aneurysm rupture while maintaining adequate end-organ perfusion. In general, the systolic BP should be kept between 105 and 115 mm Hg, the heart rate between 60 and 80 beats per minute, and the cardiac index between 2 and 2.5 L/min/m^2. Short-acting agents such as nitroglycerin, nicardipine, labetalol, or esmolol are ideal for hemodynamic control. Use of nitroprusside is discouraged because it has been associated with a higher risk of neurologic complications. For anesthetic induction, a slow technique with strict hemodynamic control is preferred. Otherwise, a "modified" rapid sequence induction can provide expeditious airway control while keeping stable hemodynamics in indicated cases. In the latter situation, acute hemodynamic changes are more prevalent and rapid titration of medications may be needed. If motor evoked potentials (MEPs) are being monitored, either succinylcholine or a short-acting nondepolarizing agent may be used to facilitate tracheal intubation. Anesthetic maintenance may be achieved using a low concentration of an inhalation agent, combined with an infusion of propofol or short-acting narcotic (e.g., sufentanil, remifentanil). If MEPs are not being monitored, the patient may be fully paralyzed, and inhalation agents with narcotics used.

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Kahn RA, Stone ME, Moskowitz DM. Anesthetic consideration for descending aortic aneurysm repair. *Sem Cardiothorac Vasc Anesth*. 2007;11:205–223.

Levine WC, Lee JJ, Black JH, et al. Thoracoabdominal aneurysm repair: anesthetic management. *Int Anesth Clin*. 2005;43:39–60.

C.5. What major organ systems are threatened during TAAA repair?

The repair of TAAA is a complex surgical procedure associated with significant multiorgan dysfunction. The main source of morbidity is end-organ ischemia. The most significant determinant of the extent and severity of organ ischemia is the aortic cross-clamp duration, and, to a lesser degree, the extension of aneurysm, which determines the anatomic placement of the aortic clamp. The aortic cross-clamp time is related to aneurysm type, complexity of the repair and surgical technique, and the surgeon's experience.

The main organ systems at risk during TAAA repair are:

- *Spinal cord*. Spinal cord injury is the most feared complication of TAAA repair. Prolonged spinal cord ischemia is the main cause of spinal cord injury, which can result in paraplegia or paraparesis. Factors contributing to spinal cord ischemia include the duration and site of placement of the aortic cross-clamp, presence of pre-existing cord ischemia, prior descending aortic aneurysm surgery, and variability in the spinal arterial supply. There are other associated factors such as reperfusion injury, local metabolic rate, and oxygen supply and demand balance.
- *Kidneys*. Risk factors associated with postoperative AKI in patients with TAAA include: age greater than 50 years, pre-existing renal insufficiency, hemodynamic instability, diffuse atherosclerosis, duration of renal ischemia (>40 minutes), and

massive transfusion. In particular, preoperative CKD or AKI present the greatest morbidity and mortality risk. The principal mechanism of kidney injury is ischemia due to aortic cross-clamping. Other forms of injury include perioperative embolic events due to aortic manipulation and the use of nephrotoxic agents (e.g., intravenous contrast dye or antibiotics).

- *Lungs*. Postoperative respiratory failure is the single most common complication of TAAA repair, occurring in 25% to 45% of patients. One of the main determinants of postoperative respiratory dysfunction is the division of the left hemidiaphragm. Even with proper isolation, the left lung parenchyma is exposed to retraction and compression during surgical dissection. Much of this manipulation occurs after the patient is anticoagulated. Tracheobronchial bleeding can significantly complicate perioperative ventilation. Other significant contributors are phrenic nerve and recurrent laryngeal nerve injuries. Excessive retraction of the lung during dissection of the aortic arch may also lead to disruption of the left main pulmonary artery and is an important cause of acute lung injury. Importantly, a significant number of patients presenting for TAAA surgery have a strong history of tobacco abuse and abnormal pulmonary function studies.
- *Mesenteric organs*. Visceral ischemia occurs with supraceliac aortic cross-clamping. An early effect is triggering of fibrinolysis. Bowel ischemia can also lead to an increase in intestinal permeability with subsequent bacterial translocation, endotoxemia, and sepsis.
- *Heart*. The presence of CAD in patients with TAAA in addition to the abrupt intraoperative changes in preload, afterload, and oxygen carrying capacity subject the heart to profound alterations in myocardial oxygen delivery and consumption. These factors, along with intraoperative acidosis, hypocalcemia, and hypokalemia, can all negatively affect myocardial contractility and conduction—increasing the incidence of perioperative myocardial ischemia or infarction and significant arrhythmias. Aortic aneurysm as well as aortic dissection are both markers of arterial stiffening and commonly associated with both isolated systolic hypertension and increased pulse pressure. Consequently, these patients may be at risk for perioperative major vascular complication due to both long-standing effects of pulsatile injury and inadequate perfusion from "diastolic hypotension." This is particularly true preoperatively where "classic" practice is to lower the systolic component to just above 100 mm Hg without any attention to the diastolic component, which can be critically low (i.e., less than 40 mm Hg).

Conrad MF, Cambria RP. Contemporary management of descending thoracic and thoracoabdominal aortic aneurysms: endovascular versus open. *Circulation.* 2008;117:841–852.

Hiratzka LF, Bakris GL, Beckman JA, et al. 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM guidelines for the diagnosis and management of patients with thoracic aortic disease: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, American Association for Thoracic Surgery, American College of Radiology, American Stroke Association, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of Thoracic Surgeons, and Society for Vascular Medicine. *Anesthesia & Analgesia*. 2010;111:279–315.

Kahn RA, Stone ME, Moskowitz DM. Anesthetic consideration for descending aortic aneurysm repair. *Sem Cardiothorac Vasc Anesth.* 2007;11:205–223.

C.6. What strategies are used for spinal cord protection?

Neurologic deficits can be seen with all types of TAAAs. More specifically, type I and II aneurysms carry the greatest risk of spinal cord injury. The incidence of paraplegia

and paraparesis is secondary to the interruption of blood supply to the spinal cord. As such, spinal cord injury is linearly proportional to aortic cross-clamp time. The risk of spinal cord injury is minimal if the aortic cross-clamp time is less than 15 minutes. In their experience with 1,509 patients, Svensson et al. reported a 20% risk of neurologic injury if aortic cross-clamp time was greater than 60 minutes and less than 10% if the surgical repair was performed in less than 20 minutes. Recent reports have identified increased risk of spinal cord injury when more than eight segmental arteries are sacrificed during TAAA repair. Other associated risk factors for perioperative spinal cord injury are emergency surgery, presence of dissection or aortic rupture, level of aortic cross-clamping, extensive disease, advanced age, and history of renal dysfunction.

The spinal cord perfusion pressure (SCPP) may be estimated as the difference between distal mean aortic pressure and cerebrospinal fluid (CSF) pressure (SCPP = MAP-CSF) (Fig. 8.9). Thus, spinal cord ischemia may be induced by perioperative hypotension, distal aortic hypotension during aortic cross-clamping, injury to the anterior spinal artery, significant increases of CSF pressure, and perioperative hypoxemia. In general, there are several different strategies for spinal cord protection: (1) maintenance of spinal cord perfusion pressure or blood flow; (2) minimization of CSF pressure; (3) attenuation of secondary spinal cord injury after primary ischemic lesion caused by interruption of blood flow; and (4) lowering of body temperature (usually accomplished by allowing "drifting" of body temperature to 34°C).

There are several techniques that can contribute to preservation of spinal cord blood flow such as proximal hypertension to increase the contribution of vertebral artery and collateral flow, reattachment of critical segmental arteries, distal aortic perfusion or LHB, and intrathecal papaverine for spinal cord arterial dilation. Otherwise, sequential aortic clamping with minimal aortic segment exclusion is effective in reducing ischemic time by moving the aortic clamp distally along the graft to restore flow to the recently attached arterial branches, and by placing the aortic clamps relatively close to each other.

The development of strategies to reduce CSF pressure was prompted by the evidence that CSF pressure rises during aortic cross-clamping. This acute increase is attributable to changes in the capacitance veins in the epidural space. The spinal veins collapse when CSF pressure exceeds spinal venous pressure. Thus, CSF drainage is used intraoperatively and postoperatively to minimize resistance to blood flow into

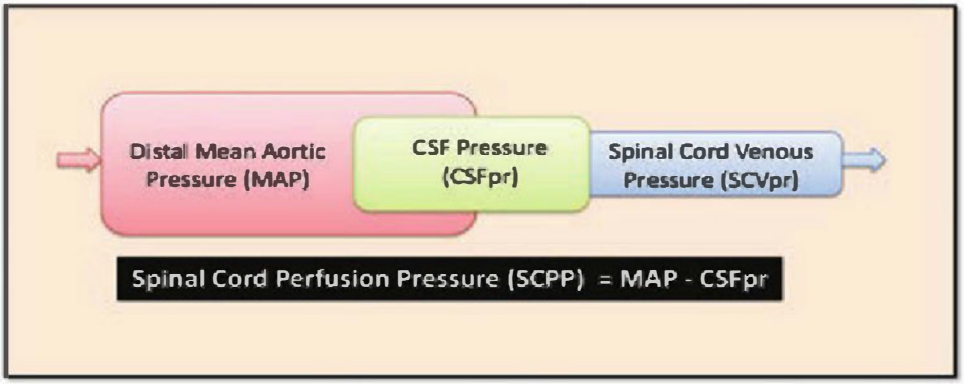

Figure 8.9 Schematic illustration of the hemodynamics governing spinal cord perfusion pressure (SCPP). The distal mean aortic pressure (MAP) must be maintained higher than the cerebrospinal fluid (CSF) pressure for adequate spinal cord perfusion. Elevation of the spinal cord venous pressure above the CSF pressure can also compromise SCPP.

the intrathecal space. In any case, oxygen delivery should be maximized with maintenance of normal hematocrit levels and Pao_2. It has also been reported that surgical retraction of the aortic arch may result in an important increase in CSF pressure.

There are various measures that increase the tolerance of the spinal cord to ischemia such as hypothermia, regional epidural cooling, and pharmacologic adjuncts including barbiturates, high-dose steroids, mannitol, and naloxone. Notably, the recently published 2010 guidelines for the diagnosis and management of patients with thoracic aortic disease recommended CSF drainage as a class I intervention for spinal cord protection in both open and endovascular TAAA repair for patients at high risk of spinal cord ischemic injury. Spinal cord pressure optimization techniques and moderate systemic hypothermia were given a level IIa recommendation. The other above-mentioned adjunctive techniques are class IIb recommendations.

- *Placement of a CSF drain*. Evidence from clinical studies supports the use of CSF drainage. One study concluded that CSF drainage resulted in an 80% reduction in the relative risk of postoperative deficits. An 18-gauge intrathecal catheter is inserted preoperatively via the L2–L3 or L3–L4 interspace. Passive continuous drainage is allowed to a CSF pressure of 8 to 10 mm Hg during the intraoperative and early postoperative period. The target pressure is raised progressively to 10 to 12 mm Hg within the first 48 hours and to 12 to 15 mm Hg once there is confirmation of preserved motor function. Complications include headache, spinal or epidural hematoma, intracranial bleeding, meningitis, and persistent CSF leaks. In this regard, excessive CSF drainage could cause cerebral hemorrhage consequent to massive intracranial fluid shifts or from tearing of cerebral bridging vessels. The rate and amount of volume removed had been found to be an independent predictor of subdural hemorrhage, which has a 50% surgical mortality. Other means of decreasing CSF pressure involve lowering the preload (by increasing drainage or pump blood flow during LHB), use of hyperosmotic agents, and hyperventilation. The potential for complications from CSF drainage limits this technique to patients at the highest risk for paraplegia (Crawford type I and II TAAAs).
- *Distal aortic perfusionc or partial LHB*. The use of LHB reduces spinal cord and mesenteric ischemic time by maintaining distal aortic perfusion. This procedure also serves to unload the left heart and control proximal hypertension during aortic cross-clamping, and enables rapid infusion of intravascular volume. Thus, it minimizes myocardial hemodynamic stress by reducing preload (potentially reducing myocardial ischemic complications) and reducing pressure on the surgeon to complete the proximal anastomosis in a short time. Patients with the most complex repairs benefit the most from LHB. In fact, a retrospective review by Coselli et al. found a reduced incidence of spinal injury only in patients with Crawford type II aneurysm. The incidence of paraplegia or paraparesis was reported as 3.9% with LHB. There are other specific circumstances in which the use of LHB offers clear benefit; anticipated technical complexity of the proximal anastomosis (such as in chronic dissection), anticipated extensive intercostal reconstruction, and involvement of a significant descending thoracic or abdominal aortic segment with possibility of performing distal aortic perfusion.
- *Hypothermia*. Moderate passive hypothermia (core body temperature 32° C to 34° C) is routinely used to limit ischemic damage mainly to the spinal cord and kidneys. This decrease of only 5° C increases the tolerable ischemic interval for the spinal cord 2.5-fold. The benefits of hypothermia are well established and are derived from a complex interaction between decreasing both the spinal cord metabolic rate and its oxygen demand, neuronal membrane stabilization, reduced excitatory neurotransmission, and optimization of microvascular flow. Longer ischemic intervals can be tolerated at lower temperatures as is evident by the use of DHCA for TAAA repair. However, lower levels of hypothermia are associated with the risk of atrial and ventricular fibrillation and other postoperative complications such as shivering, myocardial depression, and coagulopathy. Moderate hypothermia is

achieved easily by passive cooling of the patient in a cold operating room with a major incision. The use of an extracorporeal circuit allows temperature regulation in either direction. Otherwise, selective regional hypothermia can be employed inducing epidural cooling by continuous infusion of cold (at 2° C to 4° C) normal saline (via low thoracic epidural catheter) with significant reduction in the rate of postoperative neurologic deficits.

- *Reattachment of segmental arteries*. Reattachment of patent segmental intercostal and lumbar arteries in the T8 to L1 region is performed whenever feasible. This may require local endarterectomy of the artery's origin. Intercostals in the T4–T8 zone are typically oversewn, unless situated so as to be easily preserved in a beveled proximal aortic anastomosis in Crawford type I, II, or III TAAAs. More extensive reconstructions should be performed in patients with compromised collateral flow (i.e., previous history of abdominal aortic surgery or concomitant iliac aneurysm repair). Some believe that implantation of segmental vessels complicates the surgical procedure and increases the ischemic time without providing clear benefit. More importantly, the prevention of steal from the collateral network that supplies the spinal cord is achieved by temporary occlusion of segmental vessels within the open aorta.
- *Pharmacologic agents*. Several neuroprotective agents have been evaluated. Thiopental can decrease the risk of spinal cord injury by increasing the tolerance to ischemia and permitting longer periods of electrophysiologic silence. However, the use of barbiturates is limited by the high incidence of side effects from myocardial depression and vasodilation at clinically used doses. Recently, manufacturing of thiopental was discontinued and it is no longer available in the United States. A dose of methylprednisolone (30 mg/kg) before and after aortic occlusion may offer spinal protection by decreasing edema and promoting free radical scavenging. Mannitol can also decrease ischemic spinal cord injury by similar mechanisms. Naloxone is used with the purpose of decreasing the metabolic rate (inhibited neuroexcitatory state) of the spinal cord. Other substances being actively studied include memantine, allopurinol, desferrioxamine, activated protein C, insulin-like growth factor 1, riluzole, hydroxyethyl starch, adenosine, prostaglandins, and ziconotide. Of note, there is very little data in humans demonstrating efficacy of the aforementioned strategies.
- *Postoperative management*. Although a majority of spinal cord injuries occur during the procedure, up to 50% of paraplegic events may occur within the first 48 hours postoperatively in patients who had preserved somatosensory evoked potentials (SSEPs) and MEPs levels intraoperatively. In their retrospective review, Etz et al. identified both elevated central venous pressure and hypotension (relative to preoperative BP) during the first 5 postoperative hours to be statistically associated with new onset of paraplegia. Therefore, careful hemodynamic and clinical monitoring immediately after surgery may prevent some spinal cord deficits.

In summary, a multimodal approach for spinal cord protection during TAAA repair is currently the most widely recommended approach (e.g., DHCA, LHB, CSF drainage, aggressive intercostal artery reconstruction, pharmacologic adjuncts, and continuous neurophysiologic monitoring).

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Zoli S, Roder F, Etz CD, et al. Predicting the risk of paraplegia after thoracic and thoracoabdominal aneurysm repair. *Ann Thorac Surg*. 2010;90:1237–1244.

C.7. How do you detect spinal cord ischemia?

Evoked potentials may be used to continuously monitor spinal cord perfusion and detect spinal cord ischemia. These modalities of neurophysiologic monitoring are based on the detection of periodic changes of latency and amplitude as a result of a given stimulus. The signals monitored are generated by synaptic transmission of stimulus. In general, a decrease in amplitude or an increase in signal latency is an indicator of synaptic pathway disruption. In addition to ischemia, evoked potentials may also be altered by changes in temperature, anesthetic depth, and blood flow. Two varieties of evoked potentials are commonly used. *SSEPs* are recorded at the scalp as cortical signals that are stimulated at the posterior tibial or peroneal nerves. The potentials travel through the dorsal root ganglia to the posterior columns of the spinal cord and continue along the lemniscal pathways to the thalamus and the cortex. Comparison of the latency and amplitude of the potentials, tested minutes apart, define the degree of change in the SSEP. As changes in blood flow through the anterior spinal artery are not reflected in the posterior columns, it is possible to develop postoperative paralysis despite normal intraoperative SSEPs. Monitoring of SSEPs can be done until the patient is fully awake. In contrast, *MEPs* monitor the function of the corticospinal tract and anterior horn motor neurons, both areas supplied by the anterior spinal artery. The motor cortex is stimulated and the anterior tibial muscle response recorded. MEPs also have the advantage that they respond more rapidly to ischemia than SSEPs. Although injury to the motor pathways is unlikely to occur in the absence of detected changes in SSEPs, the use of only SSEPs has not improved outcomes. Most anesthetic medications decrease the amplitude of evoked potentials and increase their latency. As a general rule, potent volatile anesthetics, nitrous oxide, benzodiazepines, and barbiturates all have major effects in neurophysiologic monitoring. Conversely, opioids only

have mild inhibitory effects on SSEPs and MEPs. Obviously, muscle relaxants have severe effects on MEPs. Propofol has advantages over other anesthetic agents because, in comparison to volatile anesthetics and nitrous oxide, it produces less attenuation of SSEPs at clinical anesthetic levels. Other advantage of propofol is that it does not have a dose-dependent effect on SSEPs or MEPs. As a useful generalization, MEPs are extremely sensitive to most anesthetic agents, whereas SSEPs are only intermediately sensitive. Detection of ischemia by SSEPs, MEPs, or both during TAAA repair should prompt aggressive improvement in hemodynamics by increasing MAP (by proximal hypertension and increasing distal aortic perfusion), decreasing CSF pressure, or increasing oxygen delivery. Otherwise, it should require a modification of the surgical technique. In fact, some surgeons utilize a combination of MEPs and/or SSEPs with provocative maneuvers to induce reversible spinal cord ischemia to identify critical segmental vessels and collaterals that require re-implantation.

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C.8. What strategies are used for mesenteric and renal preservation?

A major source of morbidity related with TAAA repair is multiorgan ischemia. Specific techniques used for spinal cord protection have already been previously discussed. Several modalities provide different degrees of ischemic protection ranging from systemic protection from DHCA to other more selective approaches including the use of moderate systemic heparinization, and moderate permissive hypothermia. At an organ specific level, there are a few techniques that benefit the renal and mesenteric circulations: LHB, sequential aortic clamping, cold crystalloid renal perfusion, and selective visceral perfusion.

- *Moderate heparinization*. The administration of heparin (100 IU per kg) before aortic clamping helps prevent e3mbolization, decreases the incidence of disseminated intravascular coagulation and ultimately improves microcirculation. The use of heparin could potentially prevent thrombosis of segmental intercostal arteries, decreasing the incidence of spinal cord infarction. However, increased bleeding and coagulopathy are major disadvantages.
- *Selective visceral perfusion*. Several strategies exist for mesenteric protection. Initially, distal aortic perfusion provides blood flow to renal and mesenteric circulation during the proximal aortic anastomosis. Once the proximal anastomosis is complete, the aortic clamp is moved distally to the infrarenal aorta. Thereafter, the aneurysm is opened while the intercostals, celiac axis, and SMA are reconstructed. In order to reduce the risk of liver dysfunction, pancreatic and bowel ischemia when the aneurysm is open, separate balloon perfusion

catheters may be directly placed into each visceral artery. In the meantime, distal aortic perfusion below the level of the repair is continued. The catheters placed at the origin of the celiac axis and SMA are connected to the LHB circuit by a Y-tubing from the arterial perfusion line. These vessels are then perfused with oxygenated blood from the centrifugal pump while the proximal intercostals and visceral branches are attached to the graft, thereby reducing the mesentery ischemic time. An alternative approach is the use of right atrial–femoral arterial bypass, which has been used with or without oxygenator—like partial LHB. When this approach is selected and no oxygenator is used, blood is returned with a Pao_2 ~ 40 mm Hg (saturation 45% to 65%) and can successfully provide lower body tissue perfusion provided hemoglobin levels are maintained above 10 g/dL.

- *Renal protection*. Renal perfusion may be maintained through the use of distal aortic perfusion during the proximal aortic anastomosis. Selective renal artery perfusion improves outcomes by decreasing the incidence of postoperative AKI. This is achieved by continuous or intermittent infusion of cold (4° C) lactated Ringer's solution into the renal artery ostia when the aneurysm is open, rapidly achieving renal core hypothermia. Some institutions add 25 g of mannitol per liter and 1 g of methylprednisolone per liter to the infusion fluid, which may provide extra protection, as mannitol decreases oxygen renal demand and steroids stabilize cell membranes during the ischemic period. This technique also provides uninterrupted urine output during the procedure. Other pharmacologic adjuncts had been used for renal protection. Patients who received intravenous mannitol before and during aortic cross-clamping had better postoperative diuresis and less glomerular and renal tubular damage. In contrast, there is little evidence to support the use of furosemide as a renal protective agent during TAAA repair. Traditionally, low-dose dopamine (1 to 3 μg/kg/min) had been used due to its potential effects on renal blood flow from dilation of the renal afferent arterioles. These effects are correlated with increased urine output and creatinine clearance, but randomized clinical trials had shown that dopamine does not improve outcomes and provides no more benefit than maintenance of euvolemia during major vascular surgery. Continuous infusion of fenoldopam, a selective dopaminergic agonist, had some promising results in patients undergoing TAAA repair by promoting a more rapid return of renal blood flow and other renal performance parameters postoperatively. Finally, the traditional "clamp-and-sew" technique has been shown to be effective, in selected cases, to shorten aortic clamp times when used by experienced surgeons in referral centers.

In general, the central goal during TAAA repair is to minimize the ischemic time by performing an effective repair which can be better accomplished in a high-volume, tertiary center with availability of an experienced and dedicated operating team.

Conrad MF, Cambria RP. Contemporary management of descending thoracic and thoracoabdominal aortic aneurysms: endovascular versus open. *Circulation*. 2008; 117:841–852.

Coselli JS, LeMaire SA. Tips for successful outcomes for descending thoracic and thoracoabdominal aortic aneurysm procedures. *Sem Vasc Surg*. 2008;21:13–20.

Gleason TG, Benjamin LC. Conventional open repair of descending thoracic aortic aneurysms. *Perspect Vasc Surg Endovasc Ther*. 2007;19:110–121.

Kahn RA, Stone ME, Moskowitz DM. Anesthetic consideration for descending aortic aneurysm repair. *Sem Cardiothorac Vasc Anesth*. 2007;11:205–223.

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C.9. Describe the pathophysiology of aortic clamping and unclamping.

Response to aortic cross-clamping

The main consequences of aortic occlusion are profound hemodynamic changes. Proximal arterial hypertension is the most dramatic and consistent component of the hemodynamic response to aortic cross-clamping and is attributed to a sudden increase in afterload. During supraceliac aortic cross-clamping, venous capacitance below the clamp decreases, causing redistribution of venous blood from vascular beds below the level of the clamp. Therefore, preload acutely increases, as manifested by increases in central filling pressures. There is also an increase in contractility secondary to augmented release of catecholamines. Otherwise, there could be a decrease in heart rate. Initially, these increases in afterload, preload, and contractility result in a significant increase in myocardial oxygen consumption that can potentiate myocardial ischemia. Over time, with increasing duration of aortic cross-clamp, systemic vascular resistance increases, and cardiac output decreases. In contrast, infraceliac aortic cross-clamping has a smaller impact on arterial and myocardial filling pressures. Due to the expected sudden increase in preload upon aortic cross-clamping, the preload at time of aortic occlusion should be kept low. It is also important to attenuate the increase in proximal aortic pressure caused by the aortic clamp while considering that SCPP should not be compromised. The use of nitroglycerine for preload control and of sodium nitroprusside (SNP) for proximal arterial pressure control have been well studied. Unfortunately, there is evidence that the use of nitroglycerine alone (with no CSF drainage) and/or SNP (even with CSF drainage) may result in adverse neurologic outcome by compromising SCPP. The use of esmolol is more effective in controlling proximal arterial pressure, with greater SCPP, than the use of SNP. Another method of controlling the sudden increase in afterload is to augment the depth of anesthesia. In this setting, the use of isoflurane results in higher SCPP when compared with SNP, and is associated with a lower incidence of neurologic injury. Probably, the best results in terms of control of preload and proximal hypertension can be accomplished by the use of an extracorporeal circuit where loading conditions of the heart can be controlled by intermittent or continuous drainage into a cardiotomy reservoir. In this regard, the partial LHB circuit can provide reliable modification of these hemodynamic parameters by control of pump flow.

There are associated changes with aortic cross-clamping that occur at multiple levels.

- *SCPP or CSF pressure*. As explained previously, aortic occlusion causes an acute increase in CSF pressure, which combined with a distal decrease in MAP causes a significant decrease in SCPP. The use of vasodilators can further compromise SCPP by causing proximal and distal hypotension and also by a spinal cord blood flow steal phenomenon from the collateral network. In particular, SNP increases CSF pressure and spinal blood flow steal with potentially higher risk of adverse neurologic outcome.
- *Oxygen consumption and tissue perfusion*. Aortic pressure below the cross-clamp is directly dependent on proximal aortic pressure. Blood flow distal to the cross-clamp does not increase when preload and cardiac output are increased. Oxygen consumption below the aortic cross-clamp decreases, while oxygen uptake in tissues above the clamp increases. The subsequent imbalance between oxygen delivery and consumption and lower body hypoperfusion cause a progressive metabolic acidemia caused by increased lactate production.

Response to aortic unclamping

- *Hemodynamics*. The primary hemodynamic response to aortic cross-clamp removal is hypotension, which is attributable to: (1) central hypovolemia caused by blood volume redistribution and pooling into the reperfused tissues; (2) hypoxia-mediated

vasodilation with increased venous capacitance; and (3) release of vasoactive and myocardial-depressant metabolites from ischemic tissues, mainly lactic acid.

- *Hypoxemia*. Following cross-clamp release, a large volume of desaturated blood returns to the heart from hypoperfused tissues below the cross-clamp. However, the transit time through the pulmonary circulation may be inadequate for hemoglobin to fully saturate. The result is temporary systemic hypoxemia.
- *Metabolic*. The physiologic perturbation associated with TAAA surgery can be exaggerated as a result of tissue hypoperfusion, acid-base disturbances, hypothermia, CPB-related effects, pre-existing comorbidities, etc. As such, there should be vigilant monitoring of hemodynamics and inspection of laboratory tests to mitigate the severity of the metabolic disturbances. Severe hyperglycemia can be expected as a manifestation of significant surgical stress response. This fact could make perioperative blood glucose control difficult, more importantly in diabetic patients. Massive transfusions are accompanied by hyperkalemia, hypocalcemia, and if significant perioperative liver dysfunction is present, citrate toxicity.
- *Acidosis*. Removal of the aortic cross-clamp may therefore result in acute metabolic acidosis that may increase ventricular irritability, decrease myocardial contractility, and cause profound vasodilation. The hemodynamic changes resulting from aortic unclamping may be minimized by gradual release of the aortic cross clamp, administration of fluid and vasoactive drugs before unclamping, reducing the depth of anesthesia, and by minimizing the cross-clamp time. The goal is an expedited correction of the hypovolemia, vasodilation, and acidemia. If there is severe and persistent hemodynamic instability, the aorta can be partially or totally re-clamped while further interventions are taken and a delayed, slower clamp release can be performed.

Gelman S. The pathophysiology of aortic cross-clamping and unclamping. *Anesthesiology*. 1995;82:1026–1057.

Kahn RA, Stone ME, Moskowitz DM. Anesthetic consideration for descending aortic aneurysm repair. *Sem Cardiothorac Vasc Anesth*. 2007;11(3):205–223.

D. Postoperative Management

D.1. What are the potential complications of TAAA repair?

Morbidity and mortality are significantly higher in the elderly and in patients undergoing TAAA reoperation. Postoperative complications may include the following:

- *Myocardial infarction*. The incidence of perioperative myocardial infarction is 7% to 13%, and can result from a continued imbalance between myocardial oxygen supply and demand, especially in patients with known CAD. Pain and tachycardia can increase oxygen demands while hypoxia from respiratory dysfunction, anemia from excessive bleeding, and tachycardia can result in reduced oxygen supply to the myocardium.
- *Respiratory failure*. The likelihood of respiratory complications is increased in surgeries with thoracic and abdominal incisions. Respiratory failure occurs in up to 20% of patients following TAAA repair. Many of these patients have pre-existing pulmonary disease, which may be worsened by the sequelae of one-lung ventilation. The release of vasoactive substances from the ischemic lower extremities and lung hypoperfusion may also lead to interstitial edema. The risk of respiratory failure is increased in the elderly and in patients with a history of COPD, smoking, and cardiac or renal failure.
- *Acute kidney injury*. The incidence of AKI is 3% to 14% after TAAA repair. A cross-clamp duration greater than 30 minutes is the major determinant of postoperative

AKI. Other risk factors include age more than 50 years, CAD, diabetes, an elevated preoperative creatinine, and massive transfusion.

- *Bleeding*. The incidence of reoperation for bleeding is 3% to 5%. Causes of bleeding include heparinization, thrombocytopenia, hypothermia, acidosis, factor deficiency, disseminated intravascular coagulation, chronic hepatic or kidney disease, and coagulopathy from visceral ischemia.
- *Spinal cord injury*. The incidence of paraplegia following TAAA repair is 2% to 40%, and depends on the aneurysm type, surgical technique, and ischemia duration. Paraplegia is increased significantly with emergency surgery and cross-clamp times greater than 30 minutes. Spinal cord injury presents as loss of motor function and sensation.
- *Stroke*. The incidence of stroke following TAAA repair is reported in one series to be as high as 9.6%. However, in centers having high volume of TAAA surgery, stroke outcomes are fewer than 3%.

Acher CW, Wynn MM, Hoch JR, et al. Cardiac function is a risk factor for paralysis in thoracoabdominal aortic replacement. *J Vasc Surg*. 1998;27:821–830.

Cambria RP, Davison KJ, Zannetti S, et al. Thoracoabdominal aneurysm repair. Perspective over a decade with the clamp-and-sew technique. *Ann Surg*. 1997;226:294–305.

Godet G, Fleron MH, Vicaut E, et al. Risk factors for acute postoperative renal failure in thoracic or thoracoabdominal aortic surgery: a prospective study. *Anesth Analg*. 1997; 85:1227–1232.

LeMaire SA, Miller CC III, Conklin LD, et al. A new predictive model for adverse outcomes after elective thoracoabdominal aortic aneurysm repair. *Ann Thorac Surg*. 2001; 71:1233–1238.

E. Anesthesia for Endovascular TAAA Repair

E.1. Which patients are candidates for endovascular TAAA repair?

Endovascular TAAA repair is an alternative to conventional open surgical repair. Advantages of endovascular repair include the following: (1) it is less invasive; (2) local or regional anesthesia may be used; (3) the aorta is only briefly occluded; (4) there is minimal hemodynamic and metabolic stress; (5) the patient can ambulate and be discharged earlier; and (6) reduced hospital costs. However, not all patients are candidates for endovascular repair. Patient selection must take into account the surgical risk of "open repair" in patients with significant comorbidity. Furthermore, the proximal aneurysm neck must be at least 15 to 20 mm in length depending on the endovascular device utilized, and the maximum aneurysm diameter should be no larger than the largest available endograft. Often, to achieve sufficient proximal neck length, the left subclavian artery needs to be covered by the endograft. The distal attachment site must also be non-aneurysmal and of sufficient length to accommodate the graft. Finally, there must be at least one large, acceptable iliac artery that can be used as a conduit for graft delivery. Many patients who historically were not candidates for endovascular repair due to visceral segment involvement and/or lack of appropriate iliac artery conduit can undergo "hybrid" procedures with abdominal aortic debranching and/or surgical iliac replacement followed by endovascular repair of their TAAA. However, few long-term outcome data actually compare endovascular repair to other medical and surgical options.

Bergeron P, De Chaumaray T, Gay J, et al. Endovascular treatment of thoracic aortic aneurysms. *J Cardiovasc Surg*. 2003;44:349–361.

Hughes GC, Nienaber JJ, Bush EL, et al. Use of custom Dacron branch grafts for "hybrid" aortic debranching during endovascular repair of thoracic and thoracoabdominal aortic aneurysms. *J Thorac Cardiovasc Surg.* 2008;136:21–28.

Kahn RA, Moskowitz DM, Marin M, et al. Anesthetic considerations for endovascular aortic repair. *Mt Sinai J Med.* 2002;69:57–67.

E.2. What are the surgical steps for endovascular TAAA repair?

The most common point of access is the femoral artery. A small horizontal incision is made in the inguinal fold and the common femoral artery is exposed. Alternatively, an open approach to the iliac arteries or a percutaneous approach from the left or right brachial artery may be used. Brachial artery access is used particularly when the supra-aortic vessels need to be imaged. A puncture is made in the femoral artery and a guidewire inserted and advanced into the thoracic aorta. A 7-French diameter introducer is then placed over the guidewire. A similar introducer may also be optionally placed through the contralateral femoral artery to permit arteriography of the TAAA. The ascension of the delivery system follows removal of the 7F introducer. Once the stent-graft is properly positioned, it is then deployed. If graft extension is needed, one or more complementary stent-grafts may be deployed, with overlap of at least 2 cm between grafts. Finally, there is a global angiographic assessment for any endoleaks, with additional balloon inflation or cuff extension being performed as necessary to complete sealing. The delivery system is then removed and the arteriotomy site closed. For aortic dissections, the endoluminal graft is deployed in the true channel, covering the proximal dissection entry site. Intraoperative TEE and intravascular ultrasound are extremely helpful in confirming exclusion of the false channel.

If the aneurysm extent involves the visceral segments, abdominal debranching allows for improved aortic coverage (Fig. 8.10). In a two-stage procedure utilizing a custom Dacron graft, the visceral vessels are bypassed individually and attached to the iliac artery. This custom graft has a side port for easy inline access for endograft deployment. Typically, abdominal debranching is performed first and then endovascular repair of the aorta is performed later in a staged fashion. The technique for endovascular repair utilizing this strategy is the same as described above with the sole exception that the side port of the debranching graft may be utilized for arterial access in place of the femoral or iliac arteries (Fig. 8.11). This technique increases the availability of endovascular aneurysm repair to those who previously may have required LHB or DHCA to repair their aneurysms.

Bergeron P, De Chaumaray T, Gay J, et al. Endovascular treatment of thoracic aortic aneurysms. *J Cardiovasc Surg.* 2003;44:349–361.

Hughes GC, Sulzer CF, McCann RL, Swaminathan M. Endovascular approaches to complex thoracic aortic disease. *Semin Cardiothorac Vasc Anesth.* 2008;12:298–319.

E.3. What are the specific anesthetic considerations for endovascular TAAA repair?

The anesthetic approach for endovascular TAAA repair offers similar challenges to the traditional open procedure. In fact, candidates for endovascular repair often have more complex medical conditions and a higher perioperative risk that precludes an open surgical procedure. Although endovascular approaches are less invasive, the above-mentioned issues and the potential need to convert to open surgery warrant additional precautions. The preoperative workup of the patient scheduled for endovascular TAAA repair does not differ from that of the patient scheduled for open surgery. The main goals for intraoperative anesthetic management are to provide

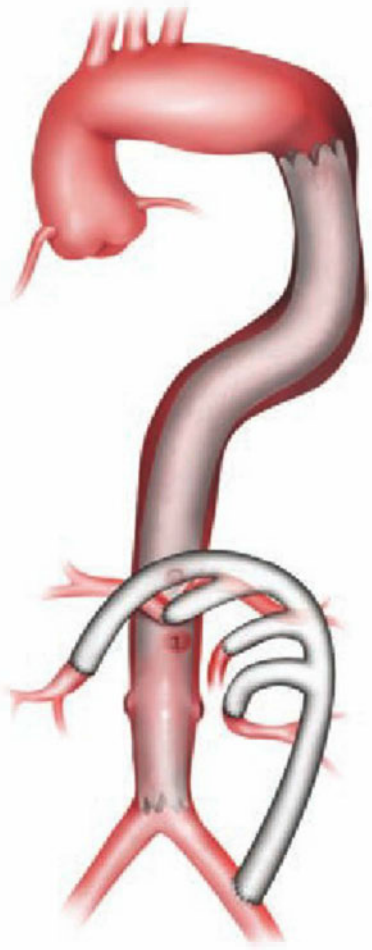

Figure 8.10 Illustration of the "hybrid" thoracoabdominal aneurysm repair with open visceral debranching and concomitant endograft-enabled aneurysm exclusion. (From Hughes GC, Sulzer CF, McCann RL, et al. Endovascular approaches to complex thoracic aortic disease. *Semin Cardiothorac Vasc Anesth*. 2008;12:298–319, with permission.)

hemodynamic stability while preserving cardiac, spinal, renal and mesenteric flow, and to maintain intravascular volume, adequate oxygenation, and normothermia. Large-bore central venous access and a right radial arterial line are recommended. Available locations for vascular access are usually limited as both groins and the left upper extremity are part of the surgical field. The femoral arteries are used for access with large-bore sheaths for both, guidewires/fluoroscopy, and the stent-graft delivery system. If required, the left arm allows proximal access via the brachial artery. Both general and regional anesthesia techniques are suitable for this procedure. General anesthesia with tracheal intubation offers the advantage of airway control in the event of emergent situations. Most commonly, general anesthetic techniques are chosen due to the increasing use of TEE and neurophysiologic monitoring during endovascular

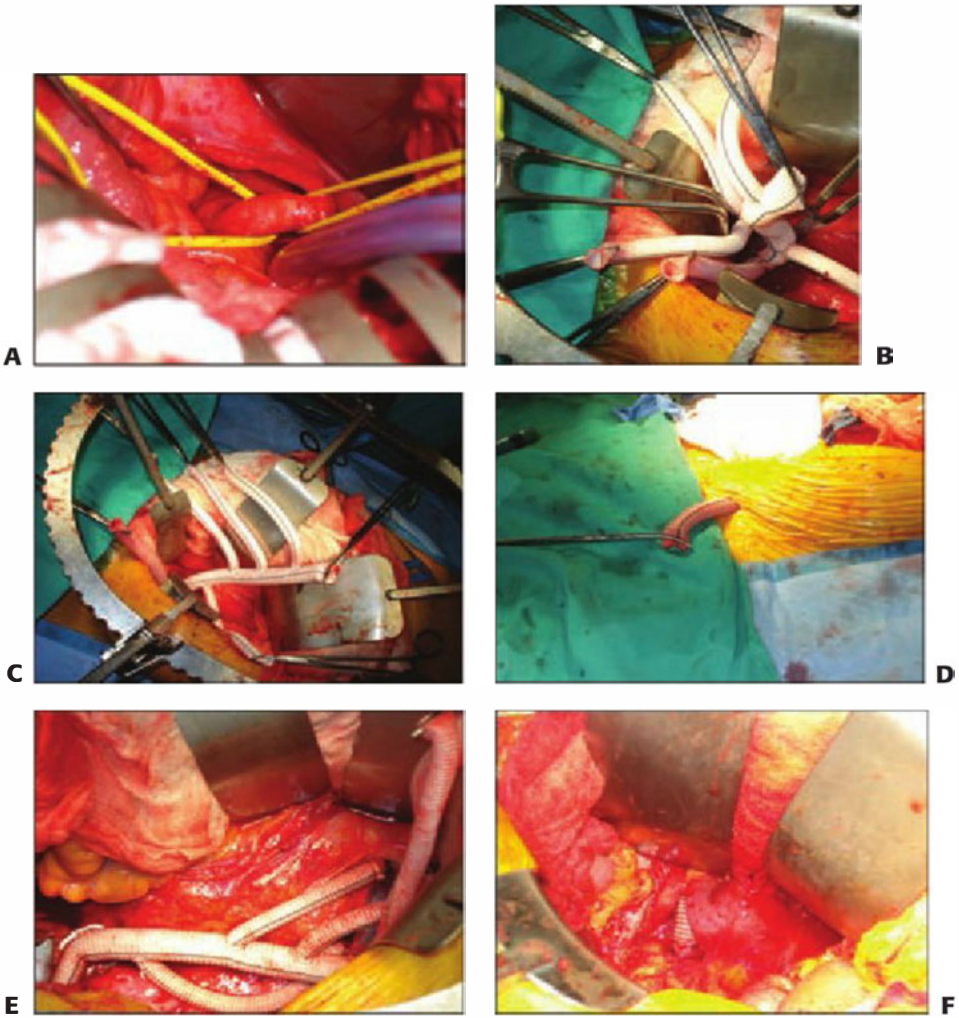

Figure 8.11 Intraoperative photographs of "hybrid" TAAA repair. **A.** The left common iliac artery has been isolated in the pelvis. **B.** The proximal anastomosis of the visceral debranching graft to the left common iliac is completed. **C.** The integral limb for the left renal artery (*bottom of photo*) is shown being put on stretch to evaluate proper length and to avoid kinking. **D.** The antegrade limb of the debranching graft for introduction of the endograft is brought out through a separate stab incision in the left lower quadrant to allow a straighter angle of entry for the endograft into the aorta. This limb will be clipped and oversewn in the abdomen at the completion of the endograft portion of the procedure. **E.** The three left-sided end-to-end anastomoses to the left renal artery, celiac axis, and superior mesenteric artery have been completed. The integral limb for the right renal artery (seen at *right of photograph*) will be tunneled through the lesser sac over to the right renal artery where it emerges beneath the inferior vena cava. **F.** View of completed right renal artery debranching in right upper quadrant of abdomen. (From Hughes GC, Sulzer CF, McCann RL, et al. Endovascular approaches to complex thoracic aortic disease. *Semin Cardiothorac Vasc Anesth.* 2008;12:298–319, with permission.)

procedures. However, regional anesthesia offers an attractive alternative in patients with reduced baseline pulmonary function.

Open and endovascular TAAA repair have comparable rates of spinal cord injury. With endovascular repair, injury is most likely the result of permanent coverage of important intercostal arteries or collaterals supplying the spinal cord. The longer the length of aorta to be covered by the stent, the higher the risk of spinal cord ischemia. According to the 2010 guidelines for the diagnosis and management of patients with thoracic aortic disease, the considerations for CSF drainage during endovascular procedures should be similar to the open approach. CSF drainage is recommended as a class I intervention for spinal cord protection in patients at high risk of spinal cord ischemic injury, regardless of type of surgical procedure.

The most critical phase of the surgical procedure is device deployment. In particular, tachycardia and hypertension should be avoided. Older-generation devices are balloon-based with a large cross-sectional area. As such, these devices are predisposed to distal migration as a result of forward aortic blood flow. Device malposition secondary to inadvertent migration may result either in occlusion of major arterial branches or incomplete aneurysm exclusion. Induced hypotension may be needed to reduce device migration. Other methods include the administration of high-dose adenosine or the induction of ventricular fibrillation to temporarily induce asystole and hence a "still" field. Newer-generation endografts are either thermally or mechanically activated ("self-deploying" stents), which do not require those maneuvers. After stent deployment, position is confirmed, and the proximal and distal ends of the graft are sealed to the aortic wall by a non-occluding endoluminal balloon. During this brief period of aortic occlusion, the patient may experience significant hemodynamic stress, especially if baseline cardiac function is poor. There are other issues specific to endovascular TAAA repair. Importantly, if there is injury of the iliac or femoral vessels, blood loss is difficult to quantify and there may be concealed retroperitoneal bleeding. Endovascular TAAA repair requires the use of substantial amounts of radiographic contrast to assist during deployment of the stent, to assess for proper positioning, to evaluate for full exclusion of the aneurysmal sac, and to exclude the presence of endoleaks. Consequently, contrast-induced nephropathy remains a significant cause of perioperative AKI, which can potentially affect long-term outcome.

TEE is an important diagnostic imaging modality during endovascular procedures for confirming aortic pathology, guiding placement of the endograft, monitoring cardiac performance, and detecting endoleaks after endograft deployment. There is some evidence suggesting that TEE is more sensitive and specific than angiography in detecting endoleaks.

"Hybrid" procedures (combined open and endovascular repairs) provide the benefits of durable repairs in patients with complex anatomy (not suitable for endovascular approach) or previous open surgery. They also reduce physiologic stress when the open approach is contraindicated due to severe comorbidities. However, hybrid procedures pose additional challenges given significant blood, fluid, and heat losses as well as increased risks of embolism, particularly when aortic arch debranching is required (Fig. 8.12). Additionally, "visceral debranching" can result in hypotension due to reperfusion with a consequently higher risk of AKI and mesenteric ischemia due to temporary ischemia and embolism.

Hiratzka LF, Bakris GL, Beckman JA, et al. 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM guidelines for the diagnosis and management of patients with thoracic aortic disease: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, American Association for Thoracic Surgery, American College of Radiology, American Stroke Association, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of Thoracic Surgeons, and Society for Vascular Medicine. *Anesthesia & Analgesia.* 2010;111:279–315.

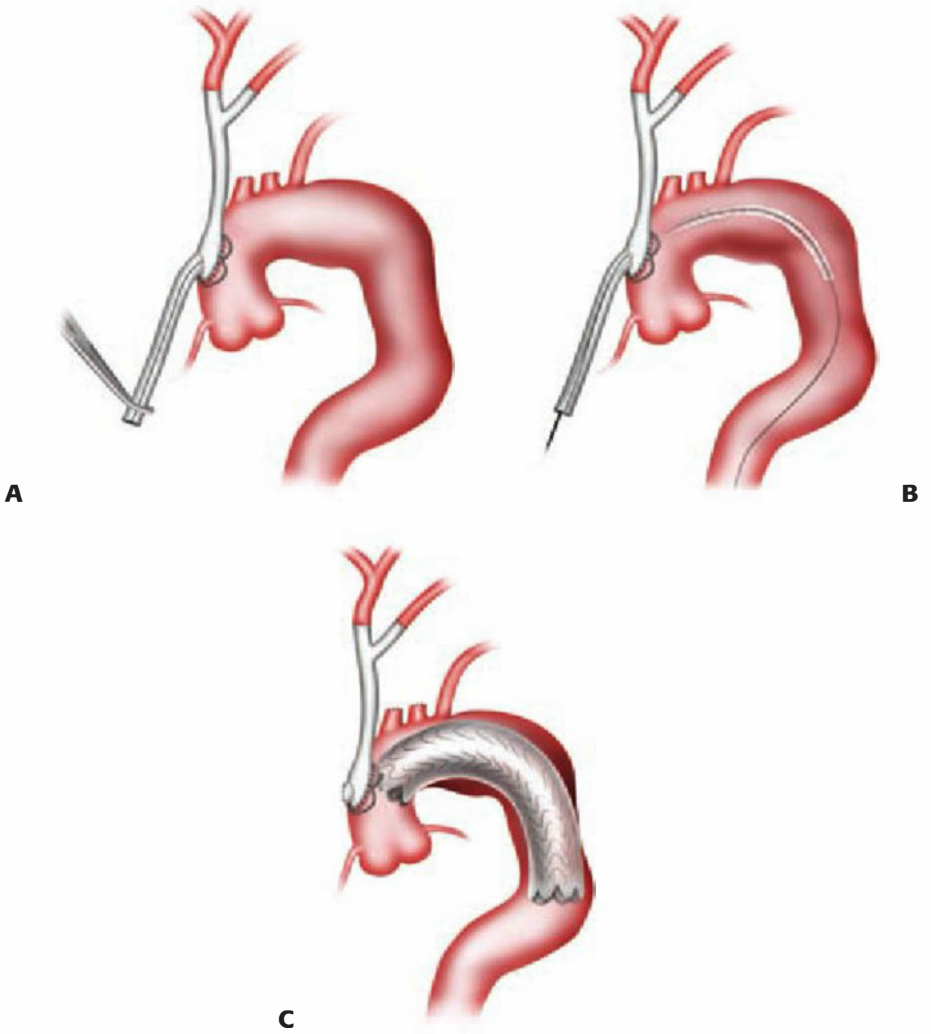

Figure 8.12 Drawing of ascending aortic based arch debranching procedure. **A.** The debranching graft has been anastomosed to the ascending aorta, left common carotid, and innominate arteries. Radiographic markers are placed around the origin of the debranching graft to facilitate identification under fluoroscopy. **B.** Endograft being introduced antegrade across the aortic arch via the integral antegrade limb of the debranching graft. **C.** Endograft has been deployed and proximal antegrade limb oversewn. (From Hughes GC, Sulzer CF, McCann RL, et al. Endovascular approaches to complex thoracic aortic disease. *Semin Cardiothorac Vasc Anesth.* 2008;12:298–319, with permission.)

Hughes GC, Sulzer CF, McCann RL, Swaminathan M. Endovascular approaches to complex thoracic aortic disease. *Semin Cardiothorac Vasc Anesth.* 2008;12:298–319.

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E.4. What are the potential complications of endovascular TAAA repair?

- *Hypotension*. The differential diagnosis of acute hypotension after stent deployment includes aortic rupture, allergic reaction to contrast dye, adenosine side effects, or sympathetic nerve blockade, if regional anesthesia is being used. The possibility of acute intraoperative aneurysm rupture is always a real risk, and the anesthesiologist must be prepared for rapid volume resuscitation, including large-bore peripheral and central venous access, arterial line, rapid infusing systems, and vasoactive agents.
- *Spinal cord ischemia*. As mentioned previously, the incidence of postoperative neurologic injury after endovascular TAAA repair is similar to that of open repair. The specific risk factors for spinal cord injury include the length of the deployed endograft and a history of previous repair. CSF drainage, avoidance of hypotension, and steroid administration are recommended in these patients. Intraoperative monitoring of SSEPs and MEPs may provide early clues of spinal cord ischemia. In these cases, pharmacologic augmentation of mean arterial pressure may improve spinal cord perfusion through collateral circulation and decrease the risk of permanent spinal cord damage.
- *Postimplantation syndrome*. This commonly observed postoperative syndrome is characterized by fever, elevated C-reactive protein levels, and leukocytosis. It is usually mild and self-limiting, lasting from 2 to 10 days. Treatment is with nonsteroidal anti-inflammatory agents.

Husain AM, Swaminathan M, McCann RL, et al. Neurophysiologic intraoperative monitoring during endovascular stent graft repair of the descending thoracic aorta. *J Clin Neurophysiol.* 2007;24:328–335.

Kahn RA, Moskowitz DM, Marin M, et al. Anesthetic considerations for endovascular aortic repair. *Mt Sinai J Med.* 2002;69:57–67.

CHAPTER 9

Abdominal Aortic Aneurysm Repair

Anup Pamnani and Lori A. Rubin

THE PATIENT IS A 76-YEAR-OLD MAN

with a 6-cm infrarenal aortic aneurysm discovered on routine physical examination and confirmed by abdominal computed tomography (CT) scan. He is a former smoker and complains of dyspnea on exertion and claudication. His electrocardiogram (ECG) shows Q waves in leads II, III, and avF; chest x-ray film displays mild hyperinflation of the lung fields; and his hematocrit is 46%. His baseline serum creatinine is 1.9.

A. Medical Disease and Differential Diagnosis

1. What are the major causes of morbidity and mortality in the patient with an abdominal aortic aneurysm (AAA)?
2. What other diseases are commonly found in patients with aortic aneurysms?
3. What is the incidence of morbidity and mortality in these patients if they undergo elective open surgical repair? What is the natural history of the disease without surgical repair?
4. What should be done for smaller aortic aneurysms that are found in patients?
5. What is the risk of perioperative myocardial infarction (MI) in patients with ischemic heart disease? What can be done to reduce the risk of ischemic events in these patients?
6. Does the morbidity and mortality of elective repair of an aortic aneurysm differ significantly from that of an emergency repair?

B. Preoperative Evaluation and Preparation

1. Which preoperative laboratory tests would you require for this patient?
2. What is the significance of the preoperative ECG? Would you wish to pursue a preoperative cardiac workup? What tests would you request, and what would they tell you?
3. Is it necessary to evaluate this patient's pulmonary status?

4. Preoperative arterial blood gas (ABG) measurement shows pH, 7.35; $Paco_2$, 47 mm Hg; and Pao_2, 68 mm Hg on room air. What is the significance of this result?
5. How would you measure creatinine clearance in this patient, and what is its value in this case?
6. Describe the blood flow to the spinal cord. What is its relevance to surgery involving the abdominal aorta?
7. How do you detect spinal cord ischemia?
8. What are the various surgical approaches to repair an AAA?
9. How does the choice of surgical technique affect the anesthetic management?
10. How would you premedicate this patient?

C. Intraoperative Management

1. Would you use an arterial line? What are the complications of arterial line placement?
2. What various monitors are available for myocardial ischemia? Is a pulmonary artery catheter (PAC) helpful in determining the occurrence of ischemia?
3. What additional monitors would you employ?
4. Is there a role for somatosensory evoked potential (SSEP) monitoring during aortic clamping?
5. How would you anesthetize this patient for an open repair of the aorta? What techniques could be used for an endovascular aortic aneurysm repair? Discuss the various anesthetic techniques that can be employed for this surgery.
6. This patient is to be heparinized intraoperatively, and anticoagulation may be continued postoperatively. Is this a contraindication to the preoperative placement of either an epidural or intraspinal catheter? What if the patient is receiving anticoagulants in the preoperative period?
7. What are your plans for fluid and blood replacement during surgery?
8. What are the hemodynamic changes of aortic cross-clamp placement? What efforts can be made to minimize these changes both before and during cross-clamping? If the patient develops ST-segment depressions with a rising pulmonary capillary wedge pressure (PCWP) during cross-clamp, what maneuvers should be taken?
9. Because this case involves an infrarenal aneurysm, is renal blood flow affected with the placement of the cross-clamp? If an endovascular repair is chosen, what are the risks to the kidneys? Are there any treatment maneuvers that can be taken to minimize these risks in either repair?
10. What are the hemodynamic consequences of aortic cross-clamp removal? What can be done to minimize the effects of removing the aortic cross-clamp? If the systemic blood pressure remains depressed after removal of the cross-clamp, what is the differential diagnosis? How would you diagnose and correct the problem?

D. Postoperative Management

1. What are the parameters used to extubate this patient?
2. What are the anticipated changes in postoperative pulmonary function in these patients? How does the surgical technique affect postoperative pulmonary function? Are there any postoperative maneuvers that can improve respiratory parameters?
3. How would you control postoperative pain? What are the alternatives in the management of this patient's postoperative pain?

A. Medical Disease and Differential Diagnosis

A.1. What are the major causes of morbidity and mortality in the patient with an abdominal aortic aneurysm (AAA)?

MI is the single most common cause of early morbidity in patients presenting for AAA resection, accounting for approximately 55% of perioperative deaths. Of all patients who suffer a perioperative MI, 70% will not survive. Other postoperative complications include bleeding, renal insufficiency, pulmonary infections and insufficiency, cerebrovascular accidents, hepatic failure, and paraplegia resulting from spinal cord ischemia. However, these events account for less than 1% of the total number of deaths from this operation. Risk factors affecting postoperative mortality are the presence of coronary artery disease (CAD), serum creatinine of greater than 1.2 mg per dL, blood urea nitrogen (BUN) greater than 40 mg per dL, age older than 60 years, emergency surgery, and indicators of poor liver function. Postoperative complications also increase with increasing transfusion requirements and emergency surgery on the abdominal aorta.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1122–1132.

A.2. What other diseases are commonly found in patients with aortic aneurysms?

The major pathologic cause of aneurysmal disease is atherosclerosis. In addition, hypertension (55%), heart disease (73.5%), peripheral vascular disease (21%), stroke and transient ischemic attacks (22%), diabetes mellitus (7%), and renal insufficiency (10%) are the most common comorbid illnesses. It is worth noting that in some studies, smoking history has been reported in as many as 80% of patients presenting for AAA repair. These risk factors, combined with advanced age (greater than 60), are exacerbated by the extreme physiologic changes that occur during aneurysmal surgery.

Cruz CP, Drouilhet JC, Southern FN, et al. Abdominal aortic aneurysm repair. *Vasc Surg*. 2001;35(5):335–344.

Ellis JE, Roizen MF, Youngberg JA. Anesthesia for abdominal aortic revascularization. In: Youngberg JA, Lake CL, Roizen MF, et al., eds. *Cardiac, Vascular and Thoracic Anesthesia*. 1st ed. Philadelphia: Churchill Livingstone; 2000:538–566.

A.3. What is the incidence of morbidity and mortality in these patients if they undergo elective open surgical repair? What is the natural history of the disease without surgical repair?

Morbidity in this patient group is most commonly due to cardiovascular, pulmonary, and renal complications. Perioperative mortality for elective open AAA repair is 2% to 5%. Increased postoperative mortality was associated with older age, elevated serum creatinine, and a lower forced expiratory volume in 1 second (FEV_1). The major cause of death in the nonsurgically treated patient is rupture with a mortality of up to 80%. Ruptured AAAs account for approximately 9,000 deaths per year in the United States. In one study, resection of AAAs doubled life expectancy. The incidence of rupture within 5 years of diagnosis of an AAA is 80%. The incidence of rupture increases with aneurysmal size: 25% for lesions of 4 to 7 cm in diameter, 45% for lesions 7 to 10 cm, and 60% for lesions larger than 10 cm. Repairing aneurysms smaller than 5.5 cm has not been shown to improve survival. Thus, only patients with aneurysms larger than 5.5 cm should be considered for surgical intervention.

After 10 years, graft patency is worse for patients with disease in distal vessels. Mortality is also increased for patients with diseased distal vessels. Survival rate is 28% in patients with isolated aortoiliac disease and increases to 41% in patients with femoral popliteal or tibial disease.

Adam DJ, Mohan IV, Stuart WP, et al. Community and hospital outcome from ruptured abdominal aneurysm within the cachment area of a regional vascular service. *J Vasc Surg.* 1999;30:922–928.

Brady AR, Fowkes FG, Greenhalgh RM, et al. Risk factors for postoperative death following elective surgical repair of abdominal aortic aneurysm: results from the UK Small Aneurysm Trial. *Br J Surg.* 2000;87(6):742–749.

Gillium RF. Epidemiology of aortic aneurysm in the United States. *J Clin Epidemiol.* 1995;48:1289–1298.

Lederle FA, Kane RL, Macdonald R, et al. Systematic review: repair of unruptured abdominal aortic aneurysm. *Ann Intern Med.* 2007;146:735–741.

A.4. What should be done for smaller aortic aneurysms that are found in patients?

Physical examination and screening, either by abdominal ultrasound or CT scan, uncover many patients with aortic aneurysms less than 5.5 cm in diameter. One study compared patients with smaller aneurysms that were followed until the aneurysm reached 5.5 cm, enlarged by more than 0.7 cm in 6 months, 1.0 cm in 1 year, or were symptomatic from their aneurysm. Mortality was the same in patients randomized to immediate repair or followed closely with no intervention. Aneurysm repair was delayed 4 years in patients who received close monitoring instead of surgical intervention. Therefore, watchful waiting is suggested for aneurysms that are smaller than 5.5 cm.

Lederle FA, Kane RL, MacDonald R, et al. Systematic review: repair of unruptured abdominal aortic aneurysm. *Ann Intern Med.* 2007;146(10):735–741.

A.5. What is the risk of perioperative myocardial infarction (MI) in patients with ischemic heart disease? What can be done to reduce the risk of ischemic events in these patients?

A retrospective analysis confirmed that cardiac mortality is high for patients who undergo vascular surgery and experience postoperative myocardial ischemia. Key factors that determine perioperative morbidity and mortality rates include the stress of surgery (aortic, peripheral vascular, emergency surgery), increased blood loss, poor preoperative cardiac functional status, history of congestive heart failure (CHF), a low ejection fraction, known CAD, and preoperative history of coronary artery bypass grafting.

The occurrence of a recent MI is an important independent predictor of perioperative morbidity and mortality. In a group of patients studied prospectively for perioperative reinfarction by Rao et al., the statistical rate of reinfarction was related to the length of time since the initial MI, decreasing to less than 2% if the infarction occurred more than 6 months earlier. Patients were monitored with PACs and arterial lines and were aggressively treated and monitored in an intensive care unit setting for 3 to 4 days postoperatively. Currently, the acute care for MI has improved and subsequent risk stratification with noninvasive testing allows for a more tailored approach to the timing of surgery in these patients.

Special consideration needs to be given to patients who have recently undergone percutaneous coronary intervention procedures for revascularization of stenotic lesions

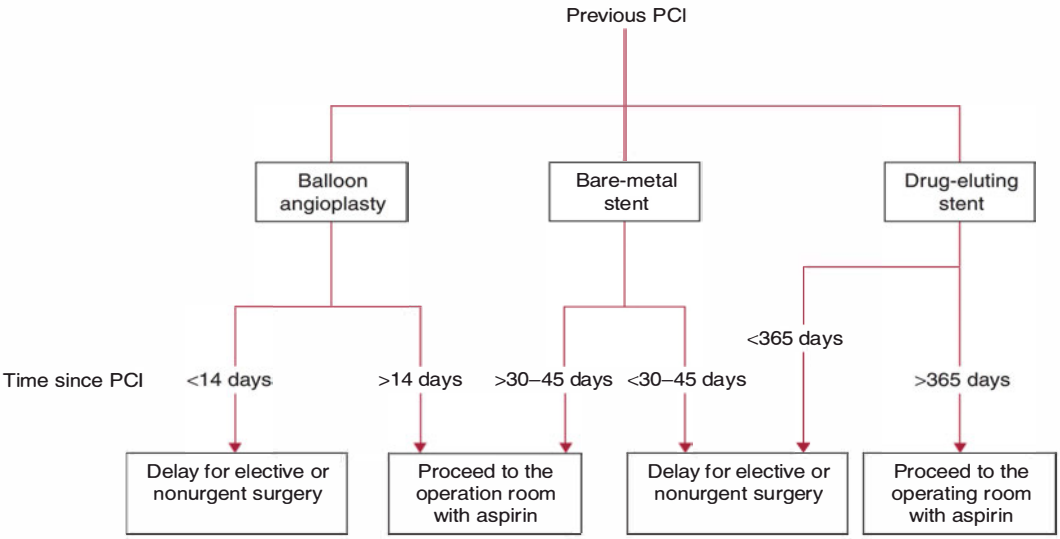

Figure 9.1 Algorithm for patients with previous percutaneous coronary interventions (PCI) for noncardiac surgery. (Adapted from Fleisher LA, Beckman JA, Brown KA, et al. 2009 ACCF/AHA focused update on perioperative beta blockade incorporated into the ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation.* 2009;120:e169–e276.)

and are being treated with platelet inhibitors (Fig. 9.1). Depending on the type of intervention undertaken, balloon angioplasty, bare metal or drug-eluting stent placement, surgery may need to be delayed for a period of 2 weeks to 1 year. This is due to the significant risk of acute stent restenosis or thrombosis in these patients if antiplatelet therapy is terminated prematurely. Caring for patients with coronary stents in the perioperative period requires input from a team consisting of anesthesiologists, surgeons, and cardiologists. The management of the dual antiplatelet therapy regimen should be customized to each patient depending on the type and urgency of surgery, type of coronary stent, time since the coronary intervention, and complexity of the coronary intervention. The current recommendations for perioperative management of patients with DES are shown in Fig. 9.2. For patients identified at high risk for stent thrombosis, surgery should be planned in a hospital with cardiac catheterization facilities. Postoperatively, these patients require a monitored setting and their antiplatelet agents restarted immediately. Signs and symptoms of stent thrombosis should be promptly recognized and aggressively treated with percutaneous coronary intervention.

In most studies, the morbidity following a perioperative MI approaches 50%. The risk after a MI may be best linked to the ongoing risk of ischemia. Patients who have survived a non-Q wave infarction are potentially at great risk for further ischemia. Badner et al. reported a 17% post-myocardial infarction mortality rate after noncardiac surgery. The mortality rate was higher if the ST segment and T-wave changes occurred during the intraoperative period. These patients should be evaluated by symptom-limited exercise testing and/or cardiac catheterization. The prevention of perioperative myocardial ischemia is the goal of the anesthesiologist regardless of the technique chosen. The basic goal is to reduce myocardial oxygen demand by avoiding tachycardia and hypertension, while increasing oxygen supply by preventing hypotension and anemia. Oxygen demand on the left ventricle is dependent on heart

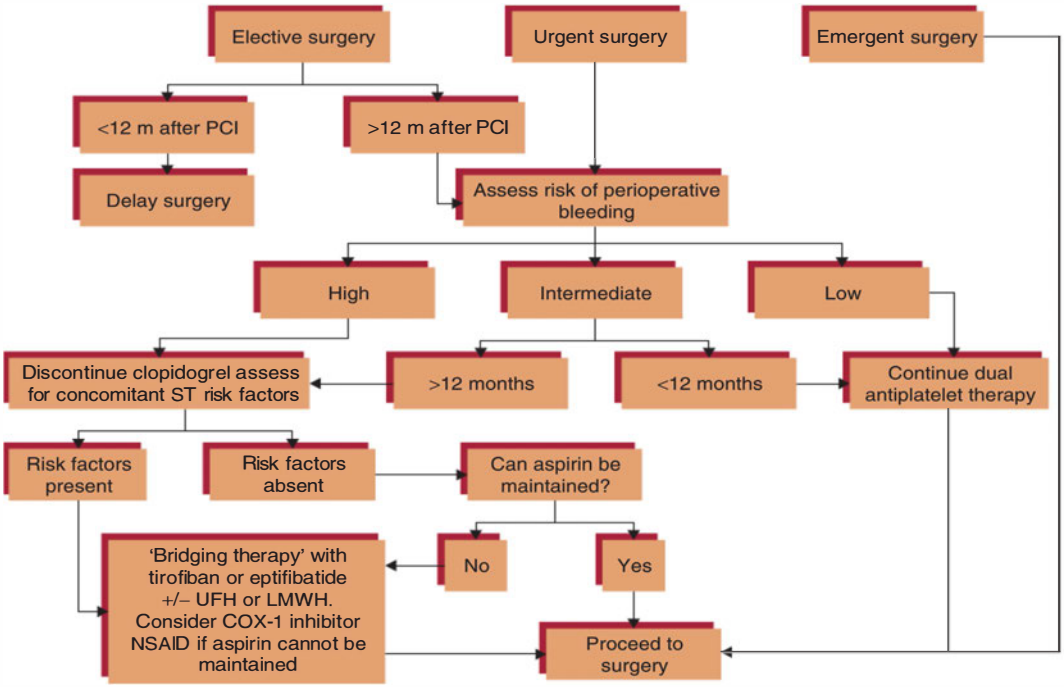

Figure 9.2 Algorithm of perioperative management of patients with DES. COX, cyclooxygenase; DES, drug-eluting stent(s); LMWH, low molecular weight heparin; NSAID, nonsteroidal anti-inflammatory drug; PCI, percutaneous coronary intervention; ST, stent thrombosis; UFH, unfractionated heparin. (From Abualsaud AO, Eisenberg MJ. Perioperative management of patients with drug-eluting stents. *J Am Coll Cardiol Intv*. 2010;3:131–142.)

rate, contractility, and the ventricular loading conditions. Of the three, the increase in heart rate imposes the greatest demand and should be readily controlled by the anesthesiologist. Left ventricular preload and afterload also affect oxygen demand by end-diastolic and systolic wall tension. Other factors, such as coronary collateral blood flow, hematocrit, and blood rheology also may influence myocardial ischemia.

β-Adrenergic antagonists are a well-established class of drugs effective in reducing myocardial oxygen consumption. Some studies suggest that β-blockers reduce perioperative ischemia and may reduce the risk of MI and cardiovascular death in patients undergoing high-risk procedures such as vascular surgery. The mechanism of reduction of myocardial oxygen consumption with β-antagonism is related to decreases in heart rate and myocardial contractility, counteracting the deleterious effects of sympathetic stimulation. In addition, this class of drugs has antiarrhythmic qualities. However, results of recent trials have not shown efficacy of high-dose, acutely administered, perioperative β-blockers to reduce overall mortality in patients undergoing noncardiac surgery. The largest of these trials, the POISE study, did show better perioperative *cardiac* outcomes with β-blocker use, however, *increased mortality* and stroke rate was also noted in the β-blocker group. Interestingly, the sub-analysis of vascular surgery patients in the study, demonstrated efficacy of perioperative β-blockers. Currently, the only class I recommendation for perioperative β-blockers use by the American Heart Association (AHA) is to continue their use in the patients who are already on β-blockers. Patients undergoing vascular surgery

who have multiple risk factors or have reversible ischemia on preoperative testing may benefit from perioperative β-blockers (class IIa). Although there are some differences between the European Society of Cardiology and the AHA guidelines, they both agree that if β-blockers are used for prophylactic purposes, they should be slowly titrated (at least a week prior to elective surgery) and acute administration of high-dose β-blockers in high-risk population is not recommended.

Nitrates also can reduce myocardial oxygen demand by decreasing preload and by dilating large epicardial coronary arteries and collateral conduit vessels. However, the benefit of perioperative nitroglycerin prophylaxis has not been proven.

The use of statins in patients with cardiovascular disease is increasingly supported by multiple studies that display a reduction in the risk of MI, stroke, and mortality. Further, accumulating data suggests that continuation of statin therapy in the preoperative period reduces the risk of postoperative death and acute coronary syndromes. The mechanisms by which statin medications attenuate cardiovascular disease extend beyond their lipid-lowering properties. In addition to anti-inflammatory and antioxidant actions, they also improve endothelial function and stabilize plaques. Thus, current American College of Cardiology (ACC)/AHA guidelines recommend continuation of statin therapy in the perioperative period.

Abualsaud AO, Eisenberg MJ. Perioperative management of patients with drug-eluting stents. *J Am Coll Cardiol Intv*. 2010;3:131–142.

Badner NH, Knill RL, Brown JE, et al. Myocardial infarction after noncardiac surgery. *Anesthesiology*. 1998;88:572–578.

Brooke BS. Perioperative beta blockers for vascular surgery patients. *J Vasc Surg*. 2010;51:515–519.

Devereaux PJ, Yang H, Yusuf S, et al. Effects of extended-release metoprolol succinate in patients undergoing non-cardiac surgery (POISE trial): a randomised controlled trial. *Lancet*. 2008;371:1839–1847.

Fleisher LA, Beckman JA, Brown KA, et al. 2009 ACCF/AHA focused update on perioperative beta blockade incorporated into the ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2009;120:e169–e276.

Lindenauer PK, Pekow P, Wang K, et al. Perioperative beta-blockade therapy and mortality after major noncardiac surgery. *N Engl J Med*. 2005;353(4):349–360.

Manach YL, Coriat P, Collard CD, Riedel B. Statin therapy within the perioperative period. *Anesthesiology*. 2008;108:1141–1146.

McFalls EO, Ward HB, Moritz TE, et al. Coronary-artery revascularization before elective major vascular surgery. *NEJM*. 2004;351:2795–2804.

Poldermans D, Bax JJ, Boersma E, et al. Guidelines for pre-operative cardiac risk assessment and perioperative cardiac management in non-cardiac surgery: the Task Force for Preoperative Cardiac Risk Assessment and Perioperative Cardiac Management in Non-cardiac Surgery of the European Society of Cardiology (ESC) and endorsed by the European Society of Anaesthesiology (ESA). *Eur Heart J*. 2009;30:2769–2812.

Popescu WM. Perioperative management of the patient with a coronary stent. *Curr Opin Anaesthesiol*. 2010;23:109–115.

Sprung J, Abdelmalak B, Gottlieb A, et al. Analysis of risk factors for myocardial infarction and cardiac mortality after major vascular surgery. *Anesthesiology*. 2000;93:129–140.

A.6. Does the morbidity and mortality of elective repair of an aortic aneurysm differ significantly from that of an emergency repair?

Overall mortality for a ruptured aortic aneurysm is greater than 50%. One study showed an overall survival rate of 19.8% as compared with an elective surgical survival rate of

95%. The worst prognosis occurred in patients older than 80 years; a systolic blood pressure of less than 80 mm Hg on admission; a prior history of hypertension, angina, or previous MI; and an operating time of greater than 4 hours. Other risk factors include a systolic blood pressure less than 100 mm Hg at the end of surgery and blood loss greater than 11,000 mL. Retroperitoneal rupture was more likely to be associated with a higher rate of survival. Elective surgical intervention should be considered if the size of the aneurysm changes rapidly or if its diameter is greater than 5.5 cm.

Ingoldby CJ, Wuyanto R, Mitchell JE. Impact of vascular surgery on community mortality from ruptured aortic aneurysms. *Br J Surg.* 1986;73:551–553.

Lambert ME, Baguley P, Charlesworth D. Ruptured abdominal aortic aneurysms. *J Cardiovasc Surg.* 1986;27:256–261.

Lederle FA, Kane RL, MacDonald R, et al. Systematic review: repair of unruptured abdominal aortic aneurysm. *Ann Intern Med.* 2007;146(10):735–741.

B. Preoperative Evaluation and Preparation

B.1. Which preoperative laboratory tests would you require for this patient?

The patient should have the following laboratory tests as part of the preoperative evaluation: complete blood count and platelet count, serum electrolytes, BUN, creatinine, coagulation profile. ABG analysis may be useful, but pulse oximetry can give similar information and $Paco_2$ may be inaccurate if the patient is hyperventilating or sedated prior to obtaining the test. Clues to the degree of chronic hypercarbia may, however, be gleaned from the serum bicarbonate value. A chest radiograph will help ascertain whether signs of heart failure or pulmonary disease are present. Further, it will help assess the degree of pulmonary dysfunction. When significant signs and symptoms of chronic obstructive pulmonary disease (COPD) are present on history and physical examination, a radiograph can help detect underlying pneumonia. In addition, a preoperative chest radiograph can help establish a baseline for comparison should pulmonary complications occur in the perioperative period. Spirometry should be considered in the patient with severe disease and those in whom an adequate medical history is not available. In addition, spirometric data may be useful in assessing the effects of inhaler therapy.

An ECG should be obtained because this patient displays multiple risk factors for ischemic disease. The ECG is a sensitive and simple screening test for active cardiac conditions, such as unstable coronary syndromes and significant arrhythmias, which necessitate further management prior to proceeding to surgery. Additionally, preoperative laboratory tests should be defined by positive findings on history and physical exam.

Roizen MF, Cohn S. Preoperative evaluation for elective surgery: what laboratory tests are needed? In: *Advances in Anesthesia*. St. Louis: Mosby-YearBook; 1993:25–48.

B.2. What is the significance of the preoperative ECG? Would you wish to pursue a preoperative cardiac workup? What tests would you request, and what would they tell you?

The patient's preoperative ECG is consistent with a prior inferior wall MI. Patients with a history of a prior MI or angina in conjunction with an abnormal ECG have a fivefold increase in postoperative mortality when compared with those with no clinical indication of CAD. His history of claudication suggests peripheral vascular disease. Patients with peripheral artery disease have a fourfold increase in risk for MI and a

twofold to threefold increase in risk of stroke than those without peripheral artery disease. If this patient's dyspnea on exertion is a symptom of CHF, this could significantly increase perioperative morbidity. In selected patients with severe or unstable cardiac ischemia, evaluation may be needed to assess if prior myocardial revascularization is indicated.

When coronary angiography was performed on 1,000 patients undergoing elective peripheral vascular surgery, it was revealed that more than half of the patients had significant CAD (greater than 50% stenosis), and 33% had severe stenosis (greater than 70%). Of the asymptomatic patients with no history or electrocardiographic evidence of ischemic heart disease, 15% had severe CAD and 22% of these seemingly normal patients had impaired left ventricular function. Hertzer et al. found that only 8% of patients undergoing elective vascular surgery had normal coronary arteries.

A comparison of this patient's current ECG with a prior ECG may aid in assessing the timing of the previous infarction if the history alone is not helpful. The 2007 update to the joint AHA/ACC guidelines concerning perioperative cardiovascular assessment suggest incorporating clinical risk factors, exercise tolerance, and surgical risk when determining whether further testing is necessary. Vascular surgeries, such as AAA repair, are categorized as high-risk procedures. In addition, clinical risk factors include a history of ischemic disease, compensated or prior heart failure, cerebrovascular disease, diabetes mellitus, and renal insufficiency. The algorithm for the cardiac assessment of patients undergoing surgical procedures associated with a high perioperative cardiac risk is shown in Figure 9.3.

Many vascular surgery patients are unable to undergo exercise stress testing because of limitations presented by their cardiac, pulmonary, or peripheral vascular disease. A dipyridamole-thallium stress test or a dobutamine stress echocardiogram is a pharmacologic test to assess ischemic potential. Dipyridamole causes vasodilation of normal coronary arteries. This results in a "steal" of blood flow from the area beyond a coronary stenosis. Blood flow redistributes as the drug dissipates.

Positive results on preoperative stress testing may not always necessitate revascularization. There is evidence to suggest that vascular patients who undergo coronary revascularization have an increased risk of periprocedural and long-term complications. The decision to perform coronary revascularization procedures, rather than employ medical management, should be undertaken in close consultation with a cardiologist and a cardiac surgeon. Recent evidence also suggests that patients at significant risk for ischemic heart disease may benefit from an endovascular approach, if anatomically feasible.

Fleisher LA, Beckman JA, Brown KA, et al. ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery). *Circulation*. 2007;116:e418–e499.

Hertzer NR, Beven EG, Young JR, et al. Coronary artery disease in peripheral vascular patients. A classification of 1000 coronary angiograms and results of surgical management. *Ann Surg*. 1984;199:223–233.

Kertai MD. Preoperative coronary revascularization in high-risk patients undergoing vascular surgery: a core review. *Anesth Analg*. 2008;106:751–758.

Sirrek CC, Watson DD, Smith WH, et al. Dipyridamole thallium-201 imaging versus dobutamine echocardiography for the evaluation of coronary artery disease in patients unable to exercise. *Am J Cardiol*. 1993;72:1257–1262.

Troisi N, Dorigo W, Lo Sapio P, et al. Preoperative cardiac assessment in patients undergoing aortic surgery: analysis of factors affecting the cardiac outcomes. *Ann Vasc Surg*. 2010;24:733–740.

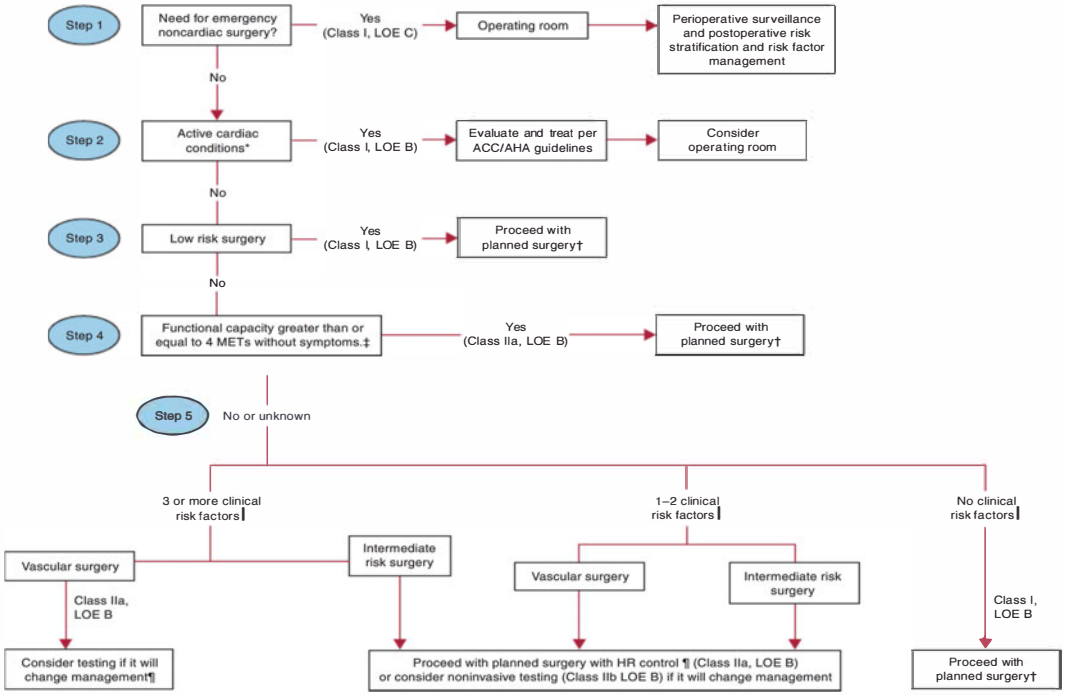

Figure 9.3 Proposed algorithm for patients undergoing surgical procedures associated with a high risk of perioperative myocardial ischemia (i.e., AAA resection). In these patients, further cardiovascular evaluation to delineate the extent of coronary artery disease (CAD) is warranted if the information obtained influences clinical care (see text). Cardiac evaluation and care algorithm for noncardiac surgery based on active clinical conditions, known cardiovascular disease, or cardiac risk for patients 50 years of age or greater. (Adapted from Fleisher LA, Beckman JA, Brown KA, et al. 2009 ACCF/AHA focused update on perioperative beta blockade incorporated into the ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: a Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2009;120:e169–e276).

B.3. Is it necessary to evaluate this patient's pulmonary status?

The patient's smoking history and the chronic changes present on his chest radiograph are evidence of COPD. Provided the patient is minimally symptomatic and has good functional status, a detailed history and thorough physical exam can provide significant information regarding pulmonary status. A chest radiograph can be particularly useful at detecting underlying lung infection. If the radiograph displays the absence of acute pulmonary processes, as in this patient, further pulmonary testing may not be indicated. In the patient with severe signs and symptoms of COPD, an ABG analysis can be particularly helpful. ABG analysis can evaluate the patient's ability to oxygenate and ventilate. Patients with severe COPD tend may be chronically hypercarbic and hypoxic. A preoperative ABG is particularly helpful at guiding perioperative ventilatory management and predicting the likelihood of postoperative mechanical ventilation in these patients.

In those patients with severe disease, particularly those with poor functional status and significant findings on physical exam and chest radiograph, pulmonary function testing may be indicated. Preoperative pulmonary function testing evalu-

ates baseline forced vital capacity (VC) and FEV_1. Maximum midexpiratory flow rate (MMEFR) is an effort-independent value that is a sensitive index of small airway obstruction. Peak expiratory flow rate is related to the FEV_1 and MMEFR, although often it is less reproducible. These tests should be performed before and after bronchodilator therapy to assess reversibility of airway obstruction. A 15% improvement is considered a positive response.

This patient is a 2-pack-per-day smoker with dyspnea on exertion and the anticipated surgery required an upper abdominal incision. These factors likely affect his baseline pulmonary function and presage postoperative ventilatory problems. A VC less than 50% of predicted, or less than 2 L total, is an indicator of increased risk of pulmonary complications as a VC at least three times the tidal volume is necessary for an effective cough. FEV_1 less than 2 L, maximum breathing capacity less than 50% of predicted, and MMEFR less than 50% of predicted are also values associated with increased risk of postoperative mechanical ventilation.

Discontinuation of smoking for 48 hours preoperatively increases oxygen tissue availability and, if stopped 4 to 6 weeks before surgery, may decrease postoperative complications. Pulmonary function tests should be viewed as a management tool to optimize preoperative pulmonary function should not be the sole means of assessing risk. Functional status, severity of illness, and comorbid medical conditions also have significant predictive value.

Kurup V. In: Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone; 2008:168–197.

Niewoehner DE. Clinical practice. Outpatient management of severe COPD. *N Engl J Med*. 2010;362(15):1407–1416.

Warner DO. Preventing postoperative pulmonary complications. The role of the anesthesiologist. *Anesthesiology*. 2000;92:1467–1472.

B.4. Preoperative arterial blood gas (ABG) measurement shows pH, 7.35; $Paco_2$, 47 mm Hg; and Pao_2, 68 mm Hg on room air. What is the significance of this result?

The normal value for Pao_2 in young adults ranges from 85 to 100 mm Hg with an average of about 95 mm Hg. This value falls steadily with aging to an average Pao_2 of 80 mm Hg at age 60. One formula for estimating Pao_2 is $Pao_2 = 100 - (\text{age in years}/3)$. The normal range for $Paco_2$ is 37 to 43 mm Hg and is unaffected by aging. For every 10 mm Hg increase in $Paco_2$, pH decreases by 0.05. For every 10 mm Hg decrease in $Paco_2$, pH increases by 0.1.

The main causes of arterial hypoxemia are hypoventilation, diffusion impairment, shunting, and ventilation/perfusion ($\dot{V}/\dot{Q}$) mismatch. The major causes of hypercarbia or carbon dioxide retention are hypoventilation and $\dot{V}/\dot{Q}$ mismatch. Mild $\dot{V}/\dot{Q}$ mismatch does not necessarily cause an increase in arterial CO_2. This is due to the fact that CO_2 is a highly diffusible gas and central chemoreceptors compensate for increasing CO_2 tension by causing an increase in ventilation. The same is not true of arterial oxygenation, however, as even mild degrees of $\dot{V}/\dot{Q}$ mismatch can lead to hypoxemia.

The assessment of this patient's blood gas analysis reveals moderate hypoxemia with a mildly elevated CO_2 tension. The pH is consistent with a mild respiratory acidosis. The most likely reason for this patient's blood gas abnormality is $\dot{V}/\dot{Q}$ mismatch, secondary to COPD, which is likely the result of his extensive smoking history.

West JB. *Respiratory Physiology*. 8th ed. Baltimore: Lippincott Williams & Wilkins; 2008:55–74.

B.5. How would you measure creatinine clearance in this patient, and what is its value in this case?

Preoperative renal dysfunction indicates potential postoperative impairment. Despite maximal medical management, including hemodialysis, acute renal failure (ARF) after aortic reconstruction carries a mortality of greater than 30% postoperatively. Maintenance of intravascular volume and adequate blood pressure are the best means of avoiding postoperative renal failure. This complication is more likely in patients requiring a suprarenal cross-clamp, but also occurs with infrarenal clamping.

Operative mortality is 19% when aortic reconstruction is performed on patients with a creatinine greater than 2 mg per dL, but mortality is only 4.6% if the levels are lower. Therefore, if the creatinine is greater than 2 mg per dL, reversible factors, such as renal stenosis, should be investigated. The most direct measurement of glomerular filtration rate (GFR) is the measurement of creatinine clearance. Although BUN and serum creatinine are related to renal function, they are altered by such nonrenal factors as protein metabolism, diet, liver dysfunction, or skeletal muscle mass. A 24-hour collection of urine is measured, and the following equation is used to calculate GFR: $GFR = U \times V/P$. U, urine concentration of creatinine (mg per dL); V, volume of urine measured (mL per minute); P, plasma concentration of creatinine (mg per dL). A 2-hour sample collected through a Foley catheter has been shown to correlate well with a 24-hour sample collection.

In spite of the widespread use of creatinine clearance to detect renal impairment, it should be noted that as much as 50% of functional nephron mass may be lost before changes in creatinine concentration become apparent. As a result, patients with lower baseline creatinine concentration can have acute kidney injury (AKI) despite normal creatinine clearance. Several novel biomarkers are being studied now that may be able to detect AKI earlier than traditional markers such as urinary output and serum creatinine. Neutrophil gelatinase associated lipocalin (NGAL) is a protein found in excess in urine and plasma in patients with AKI as many as 48 hours prior to increase in serum concentration. Serum cystatin C, a protease inhibitor that is less affected by sex, age, muscle mass, and diet than creatinine, also allows earlier detection of AKI.

Borthwick E, Ferguson A. Perioperative acute kidney injury: risk factors, recognition, management and outcomes. *BMJ*. 2010;340:c3365.

Miller DC, Myer BD. Pathophysiology and prevention of acute renal failure associated with thoracoabdominal or abdominal aortic surgery. *J Vasc Surg*. 1987;5:518–523.

Ostri P, Mouritsen L, Jorgensen B, et al. Renal function following aneurysmectomy of the abdominal aorta. *J Cardiovasc Surg*. 1986;27:714–718.

Sladen RN. Anesthetic considerations for the patient with renal failure. *Anesthesiol Clin North Am*. 2000;18:863–882.

B.6. Describe the blood flow to the spinal cord. What is its relevance to surgery involving the abdominal aorta?

The spinal cord has a system of longitudinal arteries and a system of transverse arteries as shown in Figure 9.4. Anatomic studies have shown that the most important longitudinal arteries are a single anterior spinal artery supplying 75% of the cord and a pair of posterior spinal arteries supplying 25% of the cord. Although in humans the anterior spinal artery is a continuous vessel, modern anatomy has emphasized the importance of the reinforcing transverse arteries rather than the meager longitudinal vessels. The territory supplied by the anterior spinal artery is divided into three functionally distinct levels: cervicodorsal, intermediate or midthoracic, and thoracolumbar. The cervicodorsal region receives its blood supply from the vertebral, subclavian, thyrocervical, and costocervical arteries. The midthoracic region is supplied

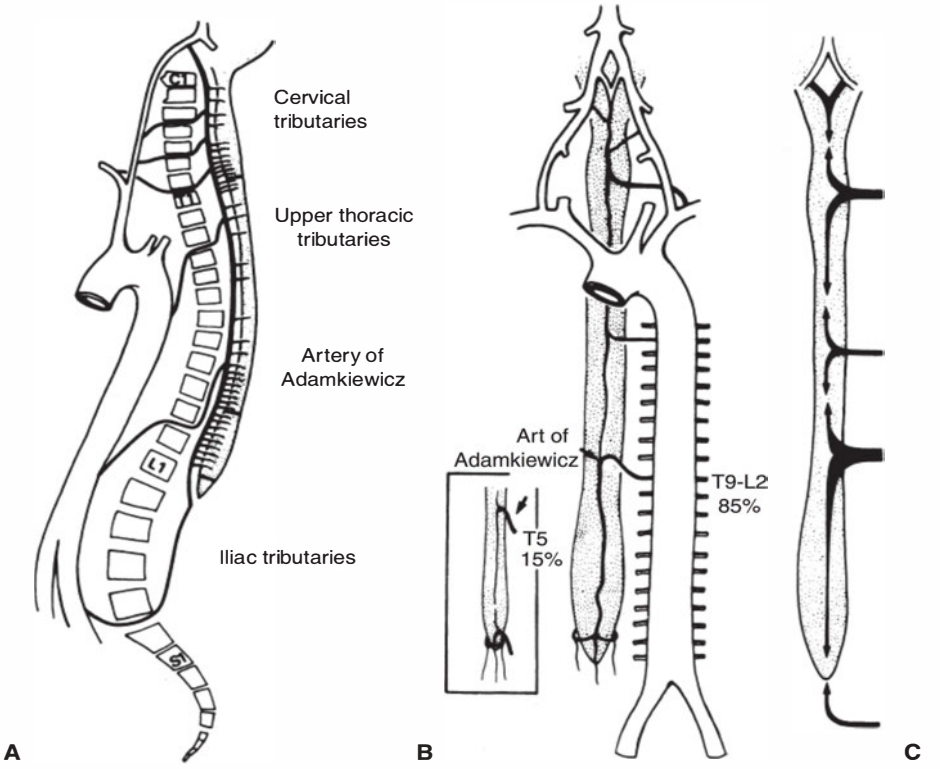

Figure 9.4 Diagram to show components of the anterior spinal artery. **A.** lateral view. **B.** Anteroposterior view showing origins of artery of Adamkiewicz. **C.** Schematic representation of direction and volume of flow from nutrient vessels supplying the anterior spinal artery. Size of arrows is proportional to flow contribution. (Adapted from Bromage PR. *Epidural Anesthesia*. Philadelphia: WB Saunders; 1978:50–54.)

by a meager left or right intercostal artery arising between the fourth and the ninth thoracic vertebrae. The thoracolumbar region of the anterior spinal artery receives its blood supply mainly from one of the intercostal arteries called the arteria radicularis magna or the artery of Adamkiewicz. It arises at the level of T5–T8 in 15%, T9–T12 in 60%, L1 in 14%, and L2 in 10% of patients. The arteria radicularis magna often is involved in the surgical repair.

The anterior spinal artery is smaller above than below the entry of the arteria radicularis magna. Resistance to blood flow is 51.7 times greater going up the anterior spinal artery as compared with coming down the artery. Therefore, distal aortic perfusion during thoracic aortic cross-clamping protects the spinal cord below the arteria radicularis magna but not above it. This is why paraplegia still occurs in approximately 2% to 15% of patients having thoracic aortic surgery with distal aortic perfusion. However, reimplantation of intercostal arteries during surgery has been shown to reduce the incidence of neurologic injury.

Spinal cord ischemia can develop during aortic cross-clamping as a result of one of two mechanisms: decreased blood flow through critical intercostal arteries (important in infrarenal cross-clamping) and hypotension in the aorta distal to the cross-clamp, leading to a "steal" phenomenon through the collateral circulation to

the distal aorta (important in thoracic cross-clamping). There are many strategies to prevent spinal cord ischemia: moderate hypothermia (local and systemic), cerebrospinal fluid drainage, and femoral–femoral bypass. The only definitive methods of preservation are fast surgery and maintenance of cardiac output.

Ling E, Arellano R. Systematic overview of the evidence supporting the use of cerebrospinal fluid drainage in thoracoabdominal aneurysm surgery for prevention of paraplegia. *Anesthesiology*. 2000;93:1115–1122.

Richenbacher J, Landolt AM, Theiler K. *Applied Anatomy of the Back*. Berlin: Springer-Verlag; 1985:268–280.

B.7. How do you detect spinal cord ischemia?

Evoked potential is used in thoracoabdominal surgery to detect spinal cord ischemia. Two varieties of evoked potential are used in thoracoabdominal aortic aneurysm repair. Somatosensory evoked potentials (SSEPs) travel through the dorsal root ganglia to the posterior columns of the spinal cord. The potentials continue along the lemniscal pathways on to the thalamus and the cortex. Comparison of the latency and amplitude of the potentials, tested minutes apart, define the degree of change in the SSEP. Temperature, anesthetic depth, and changes in blood flow can alter the evoked potentials. Changes in blood flow through the anterior spinal artery are not reflected in the posterior columns. It is possible, therefore, to have paralysis with normal SSEPs.

Ischemia of the spinal cord is indicated by increases in latency and/or decreases in amplitude of evoked potential tracing. The typical SSEP trace is shown in Figure 9.5, and its response to aortic cross-clamping is shown in Figure 9.6. The latency increases as early as 4 minutes following aortic cross-clamping, with progress to cessation of spinal cord conduction within 7 minutes of cross-clamping. Return of spinal cord conduction occurs 47 minutes following distal aortic reperfusion, with return to normal spinal cord conduction within 24 hours after operation. It has been shown that the loss of SSEP signals for longer than 14 to 30 minutes was associated with postoperative neurologic deficit.

Motor evoked potentials (MEPs) do monitor areas of the cord supplied by the anterior spinal artery. To assess motor evoked potential, patients require partial paralysis and light plane of anesthesia. Both of these requirements are suboptimal anesthetic options for a thoracoabdominal aortic aneurysm repair.

Finally, the signal-to-noise ratio of evoked potentials make interpretation of the data in the operating room more difficult and less reliable.

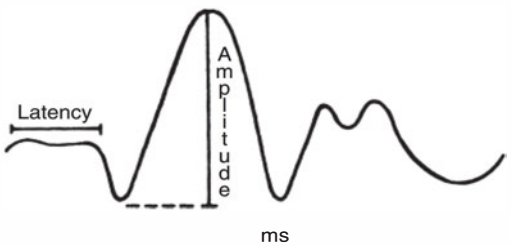

Figure 9.5 Typical somatosensory evoked potential trace. (From Cunningham JN Jr, Laschinger JC, Merkin HA, et al. Measurement of spinal cord ischemia during operations upon the thoracic aorta: initial clinical experience. *Ann Surg*. 1982;196:285–296, with permission.)

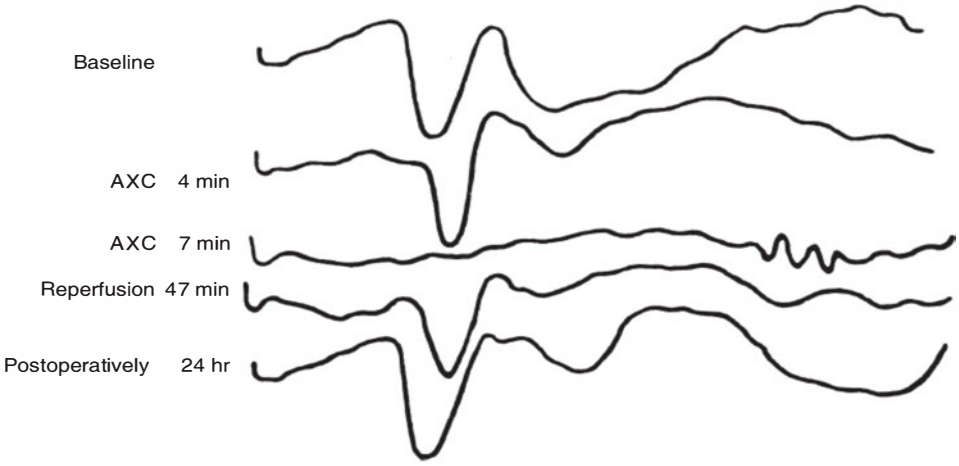

Figure 9.6 Somatosensory evoked potential response to aortic cross-clamping (AXC). (From Cunningham JN Jr, Laschinger JC, Merkin HA, et al. Measurement of spinal cord ischemia during operations upon the thoracic aorta: initial clinical experience. *Ann Surg.* 1982;196:285–296, with permission.)

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia.* 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1010,1019,1020,1038.

Coles JC, Wilson GJ, Sima AF, et al. Intraoperative detection of spinal cord ischemia using somatosensory cortical evoked potentials during thoracic aortic occlusion. *Ann Thorac Surg.* 1982;34:299–306.

Cunningham JN Jr, Laschinger JC, Spencer FC. Monitoring of somatosensory evoked potentials during procedures on the thoracoabdominal aorta: clinical observations and results. *J Thorac Cardiovasc Surg.* 1987;94:275–285.

Ginsbury HH, Shetter AG, Raudzens PA, et al. Postoperative paraplegia with preserved intraoperative somatosensory evoked potentials. *J Neurosurg.* 1985;63:296–300.

Grundy BL. Intraoperative monitoring of sensory-evoked potentials. *Anesthesiology.* 1983;58:72–87.

Meylaerts SA, Jacobs MJ, van Iterson V, et al. Comparison of transcranial motor evoked potentials and somatosensory evoked potentials during thoracoabdominal aortic aneurysm repair. *Ann Surg.* 1999;230:742–749.

B.8. What are the various surgical approaches to repair an AAA?

The classic approach to the abdominal aorta is through a vertical anterior midline incision with a transperitoneal approach to the retroperitoneal space. This gives access to all major arteries in the abdomen and pelvis. A transverse abdominal incision (supraumbilical) is also adequate for a transperitoneal approach. Although the entry is slower, there is less pain and pulmonary impairment postoperatively. The transperitoneal approach, with the necessary exposure of the abdominal organs, causes major heat and fluid loss and prolonged postoperative ileus.

The retroperitoneal approach is performed through a left flank incision with the patient in the right lateral decubitus position. In some studies, this approach has been shown to have less respiratory and wound complications, less postoperative ileus,

less blood loss, lower fluid requirements, and earlier discharge from the hospital. Monitoring and line placement must take the lateral position into consideration.

A less invasive approach to aortic aneurysm repair is endovascular aortic repair (EVAR) surgery. As stent graft technology improves, this technique is being employed in an increasing number of patients. The EVAR technique has the advantage of a shorter length of stay relative to open repair and a shortened recovery period. Due to the cost of the stents and imaging equipment, this does not necessarily translate to overall cost reduction. Anatomic issues can significantly complicate stent placement. A common problem is iliac and common femoral arteries that are of insufficient caliber. Successful aneurysm exclusion has been achieved in 50% to 90% of selected cases. Problems of the procedure include vessel perforation, inability to seal the aneurysm (endoleaks), and inability to advance the device past the iliac artery, ultimately necessitating the conversion to an open repair.

In the EVAR-1 and DREAM randomized clinical trials, reinterventions were required in two to three times as many patients in the endovascular group as in those who had open repair. Endovascular leaks are one of the leading causes of postoperative complications necessitating reintervention in up to 15% of patients. The various types of endovascular leaks are shown in Figure 9.7. In the EVAR-1 trial, postoperative complications were five times more frequent with endovascular repair when

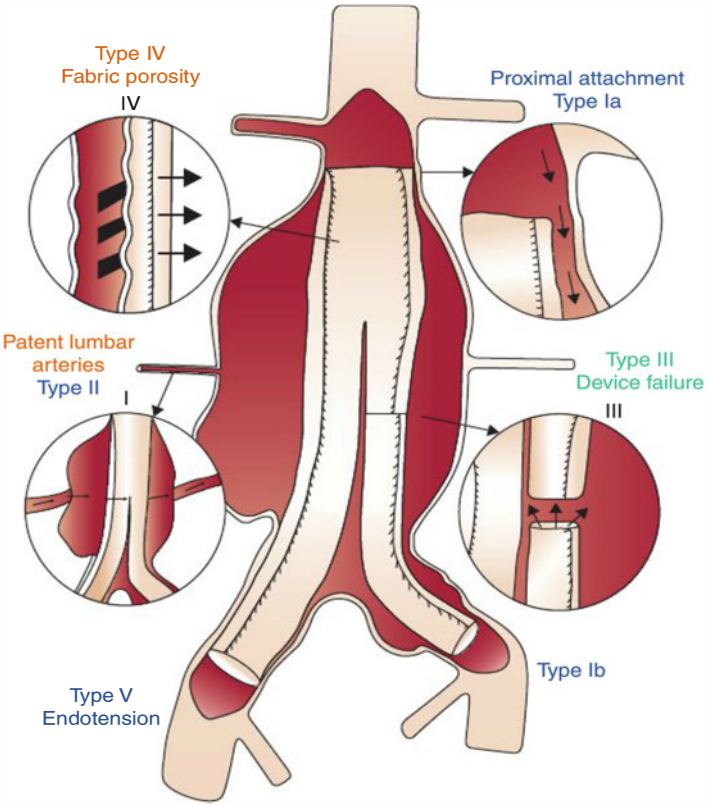

Figure 9.7 Types of endovascular leaks. (Adapted from http://www.vascular.co.nz/abdominal_aortic_aneurysms.htm. Updated July 13, 2009. Accessed June 2, 2010.)

compared to the open repair group. This highlights the importance of close follow-up in these patients and necessitates periodic reimaging for the remainder of these patients' lives. It is also worthy to note that endovascular repair has not been shown to improve survival in patients who have medical contraindication to open repair.

In contrast, when compared with open abdominal repair in the perioperative period, endovascular surgery is associated with 60% less blood loss, sooner extubation, and fewer days spent in the intensive care unit and the hospital in total. Currently, overall mortality of the procedures appears similar, and when using the Eagle criteria as a predictor of adverse cardiac events for patients undergoing major vascular surgery, it appears that a history of CHF and Q waves on ECG are predictive of cardiac events (6% in the open repair group vs. 4.8% in the endovascular group).

Ballard JL, Yonemoto H, Killeen JD. Cost-effective aortic exposure: a retroperitoneal experience. *Ann Vasc Surg*. 2001;14(1):54–58.

Dutch Randomized Endovascular Aneurysm Management (DREAM) Trial Group. A randomized trial comparing conventional and endovascular repair of abdominal aortic aneurysms. *N Engl J Med*. 2004;351:1607–1618.

EVAR Trial Participants. Endovascular aneurysm repair and outcome in patients unfit for open repair of abdominal aortic aneurysms (EVAR trial 2): randomized controlled trial. *Lancet*. 2005;365:2179–2186.

EVAR Trial Participants. Endovascular aneurysm repair versus open repair in patients with abdominal aortic aneurysm (EVAR trial 1), 30-day operative mortality results: randomized controlled trial. *Lancet*. 2004;364:843–848.

Quinones-Baldrich WJ, Garner C, Caswell D, et al. Endovascular, transperitoneal, and retroperitoneal abdominal aortic aneurysm repair: results and costs. *J Vasc Surg*. 1999;30:59–67.

Sampram ES, Karafa MT, Mascha EJ. Nature, frequency and predictors of secondary procedures after endovascular repair of abdominal aortic aneurysm. *J Vasc Surg*. 2003;37:930–937.

B.9. How does the choice of surgical technique affect the anesthetic management?

Debate exists over the advantages of general anesthesia compared with regional anesthesia or combined approaches to the management of patients with CAD. Meticulous control of heart rate and blood pressure should be the goals of any method chosen. Regional anesthesia has the potential to decrease coronary perfusion pressure as sympathetic tone is diminished and general anesthesia risks increases in sympathetic stimulation with intubation and emergence. Regional anesthesia may decrease hypercoagulability and thrombotic events in patients undergoing vascular surgery. In addition, the epidural may be used to prevent the sympathetic stimulation caused by postoperative pain.

The goals for the management of patients with CAD should include prevention and control of the effects of sympathetic nervous system stimulation. This can be achieved by using β-antagonists, narcotics, or volatile anesthetics during the perioperative period. Coronary perfusion pressure, defined as aortic diastolic pressure minus left ventricular end diastolic pressure, should be meticulously maintained. Myocardial contractility and heart rate should not be increased as this will increase oxygen demand.

DeVirgilio C, Romero L, Donayre C, et al. Endovascular aortic aneurysm repair with general versus local anesthesia: a comparison of cardiopulmonary morbidity and mortality rates. *J Vasc Surg*. 2002;36:988–991.

Ellis JE, Roizen MF, Youngberg JA. Anesthesia for abdominal aortic revascularization. In: Youngberg JA, Lake CL, Roizen MF, et al., eds. *Cardiac, Vascular and Thoracic Anesthesia.* 1st ed. Philadelphia: Churchill Livingstone; 2000:336–337.

Warltier DC, Pagel PS, Dersten JR. Approaches to the prevention of perioperative myocardial ischemia. *Anesthesiology.* 2000;92:253–259.

B.10. How would you premedicate this patient?

The most common problem a patients faces when presenting to the operating room is anxiety. Methods to relieve anxiety need to be individualized for each patient and may vary based on the preference of the anesthesiologist. Any drugs that are given should be titrated to the goals of the induction and surgery and minimize deleterious side effects. Typically, a low-dose anxiolytic is likely to be sufficient premedication for most patients. Any other preoperative medications can be given intravenously upon arrival to the operating room. If oral medications are indicated, they may be taken with a sip of water 1 hour prior to the procedure. In addition, psychological preparation for surgery is an effective technique for reducing preoperative anxiety and should be undertaken by the anesthesiologist.

Additional specific pharmacologic regimens should be tailored to individual patient needs. Various medications and combinations have been used, including narcotics, anticholinergics, barbiturates, and benzodiazepines. No single agent or combination has been demonstrated to be superior to others. Certainly, respiratory depressants should be avoided in patients who are at risk for hypoventilation (e.g., chronic CO_2 retention).

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia.* 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:836–838.

Clark SK, Rung GW, Hensley FA. Premedication for the vascular surgery patient. In: Kaplan JA, ed. *Vascular Anesthesia.* New York: Churchill Livingstone; 1991:187–204.

C. Intraoperative Management

C.1. Would you use an arterial line? What are the complications of arterial line placement?

Arterial pressure monitoring is exceedingly important in this case, from induction of anesthesia through emergence. In this patient with a history of CAD, an arterial line is particularly important for blood pressure management during induction and should be placed prior to the institution of anesthesia.

Vascular insufficiency and infection are the two major complications of arterial line placement. Catheter size and duration of cannulation are implicated in vascular occlusion. The causes of most vascular injuries are embolic. Radial artery cannulation is a low-risk, high-benefit method that can be used to closely monitor blood pressure in this patient. Open AAA repair is frequently associated with blood pressure lability, particularly on clamping and unclamping, and arterial blood pressure monitoring is particularly helpful in this situation. In addition, frequent sampling of arterial blood gases to assess hematocrit, ventilation, perfusion, electrolyte levels, glucose, and level of anticoagulation may be necessary. If a radial artery catheter cannot be placed, cannulation attempts can be made at the brachial and axillary arteries. Concerns have been raised that brachial artery cannulation might be inadvisable given the lack of adequate collateral supply to the forearm and hand. In practice, however, complications from brachial artery cannulation have been reported rarely and the risk of vascular insufficiency

appears to be no different from that of radial cannulation. Axillary artery cannulation, however, may carry an added risk of vascular insufficiency and nerve injury from thrombosis and hematoma formation. This added risk is likely due to the fact that the axillary neurovascular bundle travels in the confined space of the axillary sheath.

Barnes RW, Foster EJ, Janssen AG, et al. Safety of brachial arterial catheters as monitors in the intensive care unit—prospective evaluation with the Doppler Ultrasonic Velocity Detector. *Anesthesiology.* 1976;44:260–264.

Bedford RF. Radial arterial function following percutaneous cannulation with 18 and 20 gauge catheters. *Anesthesiology.* 1977;47:37–39.

Bedford RF, Wollman H. Complications of radial artery cannulation: an objective prospective study in man. *Anesthesiology.* 1973;38:228–236.

Slogoff S, Keats AS, Arkind C. On the safety of radial artery cannulation. *Anesthesiology.* 1983;59:42–47.

C.2. What various monitors are available for myocardial ischemia? Is a pulmonary artery catheter (PAC) helpful in determining the occurrence of ischemia?

Monitoring of the patient undergoing aortic reconstruction surgery should be aimed at preserving myocardial, pulmonary, and renal function as well as maintaining intravascular volume. Therefore, it is mandatory, particularly in the patient with known CAD, to monitor for myocardial ischemia and maintain volume status in the face of fluid shifts. Monitoring of the ST segments of the V_5 and II leads of the ECG is the most common method used to assess for intraoperative myocardial ischemia. However, in some studies, this alone was insufficient to recognize from 40% to 75% of intraoperative ischemic events detected by wall-motion abnormalities seen with a two-dimensional transesophageal echocardiogram.

Monitoring the PA pressure tracing for the appearance of V waves and increasing pulmonary capillary wedge pressure (PCWP) with decreasing cardiac output are other methods of detecting intraoperative myocardial ischemia. Unfortunately, the PAC is not a particularly sensitive technique for detecting ischemic events. Wall-motion abnormalities, detected by transesophageal echocardiography (TEE), are highly sensitive markers of myocardial ischemia and appear earlier than either ST segment or PAC waveform changes.

A microcomputer-based ECG reader (ST-segment trend monitor) also has been advocated as a monitor of myocardial ischemia. These systems can pick up more subtle changes in ST segments than by simple observation. Multilead ECG systems are most helpful. The most sensitive means for monitoring patients to determine the development of myocardial ischemia at its earliest presentation is, in fact, wall-motion abnormalities demonstrated by two-dimensional TEE. As yet, no improvement in outcome has been demonstrated by the use of any of these monitors.

ASA Task Force. Practice guidelines for pulmonary artery catheterization: an updated report by the American Society of Anesthesiologists Task Force on Pulmonary Artery Catheterization. *Anesthesiology.* 2003;99:998–1014.

ASA/SCA Task Force. Practice guidelines for perioperative transesophageal echocardiography: An updated report by the American Society of Anesthesiologists and the Society of Cardiovascular Anesthesiologists Task Force on Transesophageal Echocardiography. *Anesthesiology.* 2010;112(5):1084–1096.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia.* 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1131–1132.

Kalman PG, et al. Cardiac dysfunction during abdominal aortic operation: the limitations of pulmonary wedge pressures. *J Vasc Surg.* 1986;3:773–781.

Kotrly KJ, et al. Intraoperative detection of myocardial ischemia with an ST segment trend monitoring system. *Anesth Analg.* 1984;63:343–345.

Mangano DT. Perioperative cardiac morbidity. *Anesthesiology.* 1990;72:153–184.

C.3. What additional monitors would you employ?

An invasive monitor of volume status is recommended in patients undergoing open AAA repair. The choice of invasive monitoring, central venous pressure (CVP) or PAC can be based on the level of aortic cross-clamping and the severity of the patient's underlying cardiac disease. The CVP is informative only if it is very low or very high. As the right side of the heart is usually a compliant system, large changes in intravascular volume can occur without significant changes in the CVP. The PCWP, as obtained by a PAC, may be more accurate in determining intravascular volume status. In addition, the PAC allows for measurement of cardiac output, which may be helpful during aortic cross-clamp in the patient with left ventricular dysfunction. In this situation particularly, CVP may not accurately reflect left-sided pressures reflected by the PCWP. This is also true of the patient with significant pulmonary disease. The decision regarding placement of a PAC can also be influenced by the level at which the cross-clamp is applied. Suprarenal and supraceliac cross-clamping are associated with greater hemodynamic lability than infrarenal clamp application. Thus, PAC insertion may be of greater value during these procedures, particularly if cardiac dysfunction is also present.

In spite of all the conceptual benefits attributed to the use of PAC, evidence is lacking to recommend a reduction in morbidity and mortality associated with the use of this modality. In addition, the risk of multiple associated morbidities, including pulmonary artery rupture, arrhythmias, and complications associated with introducer placement, should be considered prior to placement of a PAC. The most recent revision of the ASA practice guidelines suggests, however, that the use of PAC may be helpful in carefully selected situations. The guidelines suggest that such monitoring may be beneficial when employed in high-risk procedures (cardiac, aortic reconstruction, anticipated hemodynamic instability, and large-volume fluid shifts), in patients with an acceptable risk for complications from catheter placement and when appropriate staff, familiar with the use and maintenance of such devices, are available. Further, when such monitoring is employed, it should only be utilized by those who are trained to interpret and intervene appropriately based on the data generated.

TEE is another monitoring modality that is being increasingly utilized in aortic reconstruction procedures. TEE has several potential benefits over other invasive monitors such as the PAC and the CVP. Currently, TEE is the most sensitive modality for detecting myocardial ischemia. It is able to detect regional wall motion abnormalities well before changes appear on other heart monitors such as the ECG or PAC. In addition, TEE allows for detailed analysis of valvular dysfunction which may significantly alter perioperative anesthetic management. In fact, certain conditions which can confound PAC data, such as systolic anterior motion of the mitral valve, severe aortic insufficiency, mitral stenosis, and severe left ventricular dysfunction, can be detected easily and quantified by TEE. The ASA practice guidelines for perioperative TEE make specific recommendations guiding the appropriate use of TEE in noncardiac surgery. According to the guidelines, the use of TEE may be appropriate when the nature of the planned surgery or the patient's known or suspected cardiovascular pathology might result in severe hemodynamic, pulmonary, or neurologic compromise. In addition, provided equipment and expertise are available, TEE should be used when unexplained life-threatening circulatory instability persists despite corrective therapy.

Another useful measure of intravascular volume status, as well as renal blood flow, is the collection of urine through a Foley catheter. Urine output will diminish with decreasing glomerular filtration caused by decreased renal blood flow. Assessment of urine output, provided kidney function is unimpaired, can be an accurate and cost-effective measure of volume status.

Temperature monitoring should also be employed as with any case under general anesthesia. Body temperature should be closely monitored and aggressively maintained. These patients can undergo tremendous heat and insensible fluid loss as a result of the enormous surface area of the bowel exposed to room air. If forced hot air thermal blankets are used, they are contraindicated on the lower extremities when an aortic cross-clamp is applied. They may, however, be used on the upper body throughout the procedure, along with fluid warmers, to maintain temperature.

Finally, pulse oximetry, capnography, and mass spectral analysis of inhaled agents also should be employed. This data combined with ABG analysis, derived from the arterial catheter, can allow for efficient ventilatory management and accurate delivery of anesthetic gases.

Ansley DM, Ramsay JG, Whalley DG, et al. The relationship between central venous pressure and pulmonary capillary wedge pressure during aortic surgery. *Can J Anaesth.* 1987;34:594–600.

ASA Task Force. Practice guidelines for PA catheterization: An updated report by the American Society of Anesthesiologists Task Force on Pulmonary Artery Catheterization. *Anesthesiology.* 2003;99:998–1014.

ASA/SCA Task force. Practice guidelines for perioperative transesophageal echocardiography: An updated report by the American Society of Anesthesiologists and the Society of Cardiovascular Anesthesiologists Task Force on Transesophageal Echocardiography. *Anesthesiology.* 2010;112(5):1084–1096.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia.* 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1122–1132.

Teplick R. Measuring central vascular pressures: a surprisingly complex problem. *Anesthesiology.* 1987;67:289–291.

C.4. Is there a role for somatosensory evoked potential (SSEP) monitoring during aortic clamping?

SSEPs can be used during aortic reconstruction surgery to monitor spinal cord function. For thoracic aortic surgery, SSEPs remain stable if the distal aortic pressure is maintained above 60 mm Hg. At lower pressures, SSEPs disappear gradually. In one study, paraplegia occurred in five of six patients whose SSEPs remained absent for more than 30 minutes. Patients should be monitored for SSEP changes if they are at higher risk of spinal cord ischemia. SSEPs are changed or lost with aortic cross-clamp most commonly in those patients who are already at increased risk for neurologic complications. Higher (especially thoracic) or prolonged cross-clamp placement also places the patient at increased risk for development of spinal cord ischemia. With a conduction block in place, such as epidural or spinal anesthesia, SSEPs will be ablated.

Ellis JE, Roizen MF, Youngberg JA. Anesthesia for abdominal aortic revascularization. In: Youngberg JA, Lake CL, Roizen MF, et al., eds. *Cardiac, Vascular and Thoracic Anesthesia.* 1st ed. Philadelphia: Churchill Livingstone; 2000:336–337.

Nuwer MR. *Evoked Potential Monitoring in the Operating Room.* New York: Raven Press; 1986:93–95.

C.5. How would you anesthetize this patient for an open repair of the aorta? What techniques could be used for an endovascular aortic aneurysm repair? Discuss the various anesthetic techniques that can be employed for this surgery.

All anesthetic techniques have been used and advocated for abdominal aortic surgery. Pure general anesthesia, combined general and regional techniques, and pure regional anesthesia all have been described. Outcome studies seem to indicate no particular difference between the techniques or agents used. Benefits and disadvantages can be argued regardless of technique, thus, allowing the anesthesiologist some flexibility in the anesthetic approach to these patients. Tailoring the anesthetic approach to the individual patient's medical condition, however, is the most effective strategy. The primary goals in the anesthetic management of patients undergoing aortic reconstruction include protection of myocardial, neurologic, and renal function. In patients with ischemic heart disease, a slow heart rate is exceedingly beneficial. Thus, anesthetic techniques in these patients should be constructed with this goal in mind.

When combined regional (epidural) and general anesthesia techniques are employed, fluid requirements may be increased in order to maintain hemodynamic stability. Typically, this additional fluid requirement can be up to 2 L per case. In addition, the sympatholysis induced by the epidural anesthetic can predispose to hypotension on clamp removal. The use of an α-agonist to provide vasoconstriction, however, can be particularly effective at counteracting the vasodilatory effects of epidural anesthesia and may reduce fluid requirements as well as episodes of intraoperative hypotension. In addition, the placement of an epidural catheter may also be of benefit for postoperative pain management of the patient.

Anesthesia for endoluminal repair has ranged from general, general combined with epidural anesthesia, lumbar epidural with sedation, or sedation with local anesthesia. Considerations for choice of anesthesia include the need to have the patient remain perfectly still for an extended period, the need for intravenous anticoagulation (heparin), the possibility of massive blood loss, and prevention of heat loss. It is important to keep blood pressure controlled during the time of balloon occlusion of the aorta to prevent distal migration of the stent. If neuraxial techniques are used, coagulation status must be carefully monitored in the perioperative period.

Baler AB. Retrospective review of 100 cases of endoluminal aortic stent-graft surgery from an anaesthetic perspective. *Anaesth Intensive Care*. 1997;25:378–384.

Baron JF, Coriat P, Mundler O, et al. Left ventricular global and regional function during lumbar epidural anesthesia in patients with and without angina pectoris: influence of volume loading. *Anesthesiology*. 1987;66:621–627.

Norris EJ, Beattie C, Perler BA, et al. Double-masked randomized trial comparing alternate combinations of intraoperative anesthesia and postoperative analgesia in abdominal aortic surgery. *Anesthesiology*. 2001;95:1054–1067.

Rupert V, Leurs LJ, et al. Influence of anesthesia type on outcome after endovascular aortic aneurysm repair: An analysis based on EUROSTAR data. *J Vasc Surg*. 2006;44:16–21.

Yaeger MP, Burns AK. Regional versus general anesthesia for major vascular surgery. In: Kaplan JA, ed. *Vascular Anesthesia*. 2nd ed. New York: Churchill Livingstone; 2004.

C.6. This patient is to be heparinized intraoperatively, and anticoagulation may be continued postoperatively. Is this a contraindication to the preoperative placement of either an epidural or intraspinal catheter? What if the patient is receiving anticoagulants in the preoperative period?

There is concern that placement of an epidural catheter in a patient to be anticoagulated increases the risk of an epidural hematoma and subsequent neurologic

deficit. For those cases in which there is significant risk of spinal cord ischemia, the diagnostic confusion of epidural hematoma versus cord ischemia may preclude the placement of an epidural catheter. However, an epidural catheter can be placed with a relative degree of confidence in patients who are not anticoagulated at the time of the puncture but who will receive anticoagulation later. Current guidelines suggest administration of intravenous heparin at least 1 hour after neuraxial catheter placement. Further, in patients who have undergone systemic heparinization, heparin should be discontinued for at least 2 to 4 hours prior to neuraxial catheter removal, coagulation status assessed before catheter manipulation, and careful assessment of the presence of sensory and motor function in the lower extremities for at least 12 hours after catheter removal.

Low molecular weight heparins (LMWHs), which are increasingly being employed for thromboprophylaxis, pose a significant potential for increased risk of neuraxial hematoma. In patients receiving these drugs, needle placement should occur at least 12 hours after the last dose of LMWH. If higher doses have been used (e.g., enoxaparin 1 mg/kg twice daily), needle placement should be delayed at least 24 hours. It is currently recommended that indwelling catheters be removed prior to initiation of LMWH thromboprophylaxis. In addition, the first dose should be administered at least 2 hours after catheter removal.

In those patients who are on chronic anticoagulation with oral warfarin, several recommendations are applicable with regard to perioperative management of neuraxial anesthesia. Oral warfarin should be discontinued at least 4 to 5 days prior to surgery. International normalized ratio (INR) should be measured at least 24 hours prior to the procedure. Neuraxial placement should only occur if INR has normalized. Neurologic testing of sensory and motor function should be performed routinely during epidural analgesia for patients on warfarin therapy. The type of analgesic solution should also be tailored to minimize the degree of sensory and motor blockade so as to allow frequent neurologic monitoring. As thromboprophylaxis with warfarin is reinitiated in the postsurgical period, neuraxial catheters should be removed while the INR is less than 1.5.

Fibrinolytic and thrombolytic drugs predispose to a high risk of hematoma formation when neuraxial anesthesia is employed. Previous guidelines based on the original contraindications for thrombolytic drugs suggested avoidance of these drugs for 10 days after puncture of noncompressible vessels. However, the third edition of ASRA practice guidelines, addressing regional anesthesia in the anticoagulated patient, recommends avoidance of all neuraxial techniques in patients who have received thrombolytic or fibrinolytic therapy. There appears to be no clear data detailing the length of time neuraxial puncture should be avoided after discontinuation of these drugs.

While the use of antiplatelet agents such as aspirin and NSAIDs do not contraindicate the use of neuraxial techniques, care should be exercised when combinations of anticoagulants and antiplatelet drugs are used. Such combinations increase the risk of hemorrhagic complications in the perioperative period and may necessitate longer waiting periods during which neuraxial puncture should be avoided after discontinuation of medications. Neurologic testing of sensory and motor function should be routinely performed on patients with indwelling catheters undergoing simultaneous anticoagulation. Again, analgesic solutions should be tailored to minimize sensory and motor changes to allow for close neurologic monitoring.

Horlocker TT, Wedel DJ, et al. Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy: American Society of Regional Anesthesia and Pain Medicine evidence-based guidelines. 3rd ed. *Reg Anesth Pain Med*. 2010;35:64–101.

Rao TLK, El-Etr AA. Anticoagulation following placement of epidural and subarachnoid catheters: an evaluation of neurologic sequelae. *Anesthesiology*. 1981;55:618–620.

C.7. What are your plans for fluid and blood replacement during surgery?

Fluid replacement should be aimed at maintaining the patient's intravascular filling pressures. The use of an invasive hemodynamic monitoring may simplify this matter greatly. In most patients, isotonic crystalloids should be used. There is little evidence to suggest that colloid administration poses any advantage over crystalloid administration.

There has been much controversy in recent literature regarding the use of "liberal" versus "restrictive" fluid protocols during open abdominal procedures. Most of this data has been gathered on patients undergoing bowel procedures, nevertheless, these models are likely applicable to the patient undergoing open AAA repair. Much of the controversy has centered on a lack of consensus regarding a predefined optimal fluid management protocol. What has emerged from this data, however, is the notion of using fluid therapy to optimize tissue perfusion rather than predefined volume replacement models.

Current paradigms for fluid management for open abdominal procedures suggest a shift away from the classic model of preoperative fluid deficit and routine replacement of high insensible losses and third space losses. Increasingly, most clinicians are employing "demand-related" regimens with the goal of maximizing tissue blood flow yet minimizing interstitial edema. Intravascular losses are replaced by timely fluid and blood product administration as measured by visual blood loss, vital signs, urinary output, hematocrit and acid–base status, and invasive hemodynamic monitoring (as available). Insensible losses are replaced at a significantly lower rate, typically 0.5 to 1 mL/kg/hr, than the traditionally higher estimates previously used. Further, the traditional concept of a third-space compartment is increasingly being abandoned. Instead, it is now being recognized that fluid shift into the interstitium is primarily related to crystalloid overload and deterioration of vascular permeability. Thus, fluid regimens should be tailored toward judiciously maintaining intravascular volume while minimizing edema rather than filling a theoretical compartment that does not appear to exist.

The concurrent use of an autotransfuser (e.g., Cell Saver) decreases the need for homologous blood transfusions. Overtransfusion of blood products should be avoided because multiple long-term complications, such as delayed hemolytic transfusion reaction, immune suppression, transmission of infectious organisms and lung injury, have been associated with blood product administration. With the hemodynamic changes associated with aortic cross-clamping, it is vital to maintain adequate intravascular volume to ensure adequate renal perfusion and normotension after removal of the cross-clamp.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1131–1132.

Chappell D, Jacob M, Hofmann-Kiefer K, et al. A rational approach to perioperative fluid management. *Anesthesiology*. 2008;109:723–740.

Grocott MP, Mythen MG, Gan TJ. Perioperative fluid management and clinical outcome in adults. *Anesth Analg*. 2005;100:1093–1106.

Jacob M, Chappell D, Rehm M. Clinical update: perioperative fluid management. *Lancet*. 2007;369:1984–1986.

C.8. What are the hemodynamic changes of aortic cross-clamp placement? What efforts can be made to minimize these changes both before and during cross-clamping? If the patient develops ST-segment depressions with a rising pulmonary capillary wedge pressure (PCWP) during cross-clamp, what maneuvers should be taken?

The systemic hemodynamic response to aortic cross-clamping is shown in Figure 9.8.

Arterial hypertension is the most dramatic and consistent result of the application of an aortic cross-clamp. This is easily envisioned as a result of a sudden increase

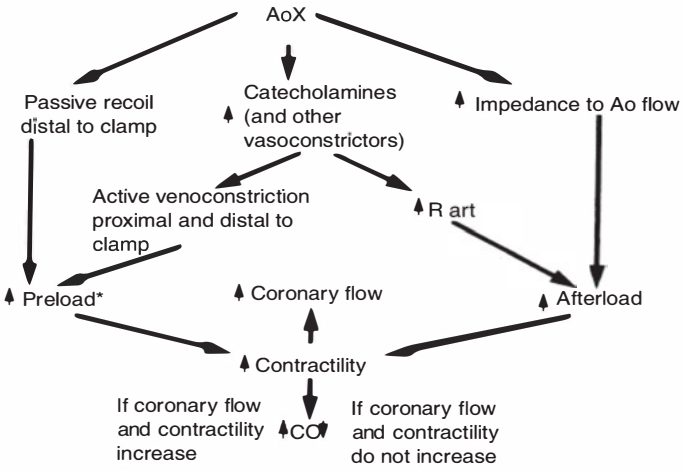

Figure 9.8 Systemic hemodynamic response to aortic cross-clamping. Ao, aortic; AoX, aortic cross-clamping; R art, arterial resistance; ↑ and ↓ , increase and decrease, respectively. *Different patterns are possible. (From Gelman S. The pathophysiology of aortic cross-clamping, and unclamping. *Anesthesiology*. 1995;82:1026-1060, with permission.)

in afterload resulting in increased left ventricular end-diastolic wall stress and systemic arterial pressure. Usually these changes are accompanied by decreased cardiac output. Some of these changes may also be due to redistribution of blood volume from the venous vasculature to the upper part of the body. All of the previously stated factors are more profound in the case of supraceliac or thoracic cross-clamp placement. Variations in blood volume status or splanchnic vascular tone are affected by the depth of anesthesia, type of anesthestic, and intravascular volume status. These factors all help determine the pattern of blood volume redistribution.

A sudden increase in afterload can lead to left ventricular failure, particularly in the patient with a noncompliant left ventricle. Ideally, the patient should have lower filling pressures for the half hour prior to cross-clamp placement. This helps to minimize the adverse response to the sudden increase in afterload. The PAC is helpful in accurately assessing and maintaining preclamp values for the left side of the heart. A potent anesthetic agent and/or a vasodilator such as nicardipine is used to return afterload to near normal. This also helps increase the cardiac output and decrease stress on the left ventricle. If this is insufficient to reverse left ventricular failure, the addition of an inotrope may be necessary.

The increase in afterload, following cross-clamp placement, may also result in myocardial ischemia. Ischemia, reflected as a rising PCWP and ST-segment depressions, can be managed with intravenous nitroglycerin, a potent dilator of the capacitance vessels. This drug is used to decrease left ventricular end-diastolic volume and left ventricular end-diastolic pressure. Decreasing left ventricular end-diastolic pressure also decreases the transluminal pressure across the coronary vasculature. This increases blood flow to the myocardium.

Ellis JE, Roizen MF, Youngberg JA. Anesthesia for abdominal aortic revascularization. In: Youngberg JA, Lake CL, Roizen MF, et al., eds. *Cardiac, Vascular and Thoracic Anesthesia*. 1st ed. Philadelphia: Churchill Livingstone; 2000:538–566.

Gelman S. The pathophysiology of aortic cross-clamping and unclamping. *Anesthesiology*. 1995;82:1026–1060.

C.9. Because this case involves an infrarenal aneurysm, is renal blood flow affected with the placement of the cross-clamp? If an endovascular repair is chosen, what are the risks to the kidneys? Are there any treatment maneuvers that can be taken to minimize these risks in either repair?

ARF after aortic aneurysm repair is associated with a mortality of greater than 30%. Decreased renal function is observed in many patients after aortic cross-clamping, even when the clamp is placed distal to the renal arteries. Although it is clear that a suprarenal cross-clamp will decrease renal blood flow up to 80%, an infrarenal cross-clamp also causes a decrease in renal cortical blood flow with an associated decrease in GFR. The degree of decrease in urine output does not correlate with the decrease in GFR nor does it predict postoperative renal failure. The most dangerous complication of alteration in renal blood flow is acute tubular necrosis and ARF.

The maintenance of cardiac output and adequate circulating blood volume is of prime importance in sustaining renal blood flow and in the prevention of renal failure. Low-dose dopamine (2–3 μg/kg/min) increases renal blood flow and may improve urine output, although decreased incidence of postoperative renal failure has not been proven. Renal protection may, however, be provided by the administration of mannitol (0.25 g/kg). The use of mannitol attenuates the reduction of renal cortical blood flow before, during, and after renal ischemia, causes a concurrent increase in glomerular ultrafiltration pressure, which increases the GFR, and is a hydroxyl free radical scavenger. Drugs such as fenoldopam and furosemide are also occasionally used during aortic reconstruction procedures with the hope of preventing renal injury. Unfortunately, strong clinical evidence is currently lacking for any of these measures.

During endovascular repair, the use of radiocontrast material may cause further insult to the kidneys. There is some suggestion that the use of a bicarbonate infusion or pretreatment with N-acetyl cysteine maybe protective. It is prudent to minimize the use of nonionic contrast or to use gadolinium dimeglumine if possible for imaging.

Alpert RA, Roizen MF, Hamilton WK, et al. Intraoperative urinary output does not predict postoperative renal function in patients undergoing abdominal aortic revascularization. *Surgery*. 1984;95:707–710.

Gamulin Z, et al. Effects of infrarenal aortic cross-clamping on renal hemodynamics in humans. *Anesthesiology*. 1984;61:394–399.

Merten GJ, Burgess WP, Gray JV et al. Prevention of contrast-induced nephropathy with sodium bicarbonate: a randomized clinical trial. *JAMA*. 2004;291(19):2328–2334.

Miller DC, Myers BD. Pathophysiology and prevention of acute renal failure associated with thoracoabdominal or abdominal aortic surgery. *J Vasc Surg*. 1987;5:518–523.

Paul MD, Mazer CD, Byrick RJ, et al. Influence of mannitol and dopamine on renal function during elective infrarenal aortic clamping in man. *Am J Nephrol*. 1986;6:427–434.

Youngberg JA, Lake CL, Roizen MF, et al. *Cardiac, Vascular, and Thoracic Anesthesia*. New York: Churchill Livingstone; 2000:557–559.

C.10. What are the hemodynamic consequences of aortic cross-clamp removal? What can be done to minimize the effects of removing the aortic cross-clamp? If the systemic blood pressure remains depressed after removal of the cross-clamp, what is the differential diagnosis? How would you diagnose and correct the problem?

The hemodynamic response to aortic unclamping is shown in Figure 9.9.

During cross-clamping, blood flow to the lower extremities is grossly decreased. Metabolism switches from aerobic to anaerobic as ischemia develops. This results in maximal vasodilation and lactic acid production. When the cross-clamp is released,

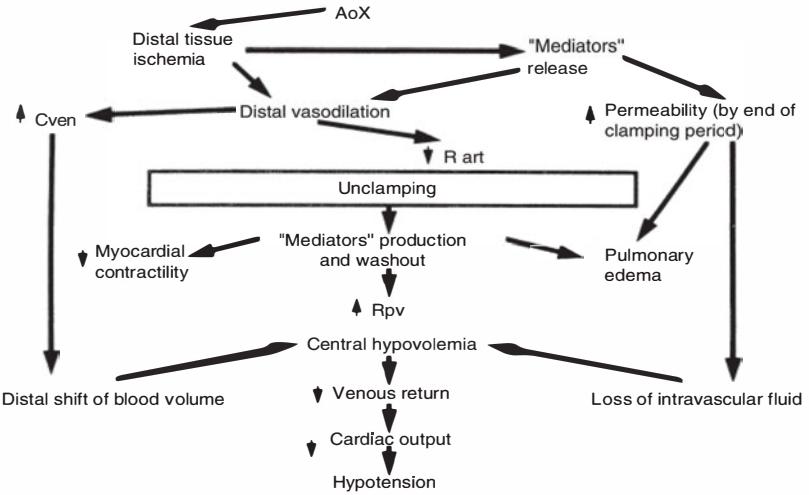

Figure 9.9 Systemic hemodynamic response to aortic unclamping. AoX, aortic cross-clamping; Cven, venous capacitance; R art, arterial resistance; Rpv, pulmonary vascular resistance; ↑ and ↓, increase and decrease, respectively. (From Gelman S. The pathophysiology of aortic cross-clamping and unclamping. *Anesthesiology.* 1995;82:1026–1060, with permission.)

systemic vascular resistance and arterial blood pressure decreases dramatically. Reactive hyperemia is a consequence of unclamping. This may be the result of arterial relaxation (myogenic mechanism), an accumulation of vasodilating substances below the occlusion, or anoxic relaxation of smooth muscles. Peripheral vasodilation can result in relative volume depletion and hypotension. Vasodilation may become systemic as the lactic acid is washed out of the extremities into the central circulation. This condition is sometimes known as "declamping shock."

To minimize the hypotensive response, volume loading in the period prior to cross-clamp release is suggested to raise filling pressures to slightly above normal. Vasodilators such as nitroprusside and/or nitroglycerin during this period allow additional volume loading with maintenance of filling pressures. In addition, gradual release of the clamp allows time for adjustments in volume, pressors, and correction of acidosis.

Sometimes, even in the face of adequate volume loading, the blood pressure remains low following cross-clamp removal. The more cephalad the cross-clamp is placed, the greater the incidence of this problem. In this situation, it is advisable to ask the surgeon to reapply the aortic cross-clamp to varying degree depending on the severity of hypotension. Such maneuvers allow more time for correction of blood volume or acidosis.

Other causes of sustained hypotension in the face of adequate management include a continued site of hemorrhage and myocardial ischemia and/or failure. Measurement of filling pressures or use of TEE can particularly help in the differentiation of the etiology of sustained hypotension. Ischemia or failure can be detected by wall motion abnormalities or elevated filling pressures accompanying systemic hypotension. In contrast, hemorrhage is diagnosed by low filling pressures and increased systemic vascular resistance (due to reflex vasoconstriction).

Eklof B, Neglen P, Thomson D. Temporary incomplete ischemia of the legs induced by aortic clamping in man: effects on central hemodynamics and skeletal muscle metabolism by adrenergic block. *Ann Surg.* 1981;193:89–98.

Gelman S. The pathophysiology of aortic cross-clamping and unclamping. *Anesthesiology*. 1995;82:1026–1060.

Reiz S, Peter T, Rais O. Hemodynamic and cardiometabolic effects of infrarenal aortic and common iliac artery declamping in man: an approach to optimal volume loading. *Acta Anesth Scand*. 1979;23:579–586.

D. Postoperative Management

D.1. What are the parameters used to extubate this patient?

Once the patient is awake and alert, has an adequate gag reflex and displays signs of adequate reversal of neuromuscular blockade, the following ventilatory criteria can be used to assess suitability for extubation: The patient is suitable for extubation once he is awake and alert, has an adequate gag reflex, displays signs of adequate reversal of neuromuscular blockade, and meets minimum respiratory parameters for extubation. The typical respiratory parameters used to assess suitability for extubation are shown in Table 9.1.

It is important to recognize that such parameters should serve merely as a guide in the clinical assessment of suitability for extubation. The decision to extubate ultimately should be guided by assessment of the patient's overall status and clinical judgment. Extubation may need to be delayed in those patients who display labored breathing on physical exam, inadequate pain control, or hemodynamic instability.

Perioperative fluid management also should be carefully considered when assessing a patient's suitability for extubation. For shorter cases with minimal anticipated fluid shifts, the patient can be extubated in the immediate postoperative period. For longer cases, instances of large volumes of fluid replacement and significant blood product administration, extubation should be delayed until the hemodynamics are stabilized and temperature is normalized. In these cases, airway swelling also can be a significant concern and may lead to ventilatory failure in the postoperative period. A "cuff leak" test may be somewhat indicative of the degree of airway edema. It is performed by occluding the endotracheal tube of a spontaneously breathing patient and auscultating for breath sounds with the cuff deflated.

Kurup V. In: Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Coexisting Disease*. 5th ed. Philadelphia: Churchill Livingstone; 2008:184–191.

Table 9.1 Typical Respiratory Parameters Used to Determine Suitability for Extubation

Vital capacity greater than 15 mL/kg
pH greater than 7.30
Pa_{O_2} greater than 60 mm Hg at F_{IO_2} less than 50%
Pa_{CO_2} less than 50 mm Hg
Maximal negative inspiratory force greater than −20 cm H_2O
Stable hemodynamic status
Respiratory rate less than 30 breaths per minute

D.2. What are the anticipated changes in postoperative pulmonary function in these patients? How does the surgical technique affect postoperative pulmonary function? Are there any postoperative maneuvers that can improve respiratory parameters?

The transabdominal approach to the aorta involves an upper abdominal incision. Total lung capacity and its subdivisions decrease after upper abdominal surgery. VC decreases 25% to 50% and returns to normal in 1 to 2 weeks, and residual volume increases 13%. Functional residual capacity declines 30% and recovers over 3 to 4 days. Expiratory reserve volume declines 20% after lower abdominal surgery and up to 60% after upper abdominal and thoracic incisions. Tidal volume decreases 20% on the first postoperative day and gradually returns to normal. The retroperitoneal approach to the aorta involves a flank incision, which leads to far less respiratory compromise.

In a series of adult men undergoing abdominal surgery, postoperative pulmonary complications occurred more frequently than cardiac complications (9.6% vs. 5.7%) and were associated with significantly greater length of hospitalization. Many of these complications are related to disruption of the normal activity of the respiratory muscles, from the beginning of the anesthetic to the postoperative period. In addition, the effects of surgical trauma are most pronounced after upper abdominal surgery. Lower abdominal and thoracic incisions impact the respiratory muscles to a lesser degree. This occurs through surgical disruption of the respiratory muscles, postoperative pain, and abdominal contents, preventing normal movement of the diaphragm. The resulting respiratory pattern is that of shallow rapid breaths without sighs.

Although regional anesthetic techniques have the potential to improve pain and reflex inhibition of respiratory muscles, they also may significantly alter postoperative respiratory muscle function. The overall effect of postoperative regional analgesia on the pattern of breathing may be complex, but it is thought that epidural analgesia may decrease the risk for postoperative pulmonary complications. Ambulation and control of postoperative pain diminish splinting and help maximize respiratory parameters. Maneuvers to encourage deep breathing are of proven benefit.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1122–1132.

Warner DO. Preventing postoperative pulmonary complications. The role of the anesthesiologist. *Anesthesiology*. 2000;92:1467–1472.

D.3. How would you control postoperative pain? What are the alternatives in the management of this patient's postoperative pain?

The goal of effective postoperative pain relief is to produce a high quality of pain control with the fewest number of side effects and complications. Neuraxial analgesia in the immediate postoperative period is the preferred method of pain management in this high-risk patient population. The ideal opiate, its concentration, and combination with local anesthetic have yet to be defined. (For suggested protocols, see Table 9.2.)

Complications of the epidural route of analgesia include dural puncture, epidural hematoma, and epidural abscess. The risk of epidural hematoma is small in patients receiving appropriate doses of anticoagulation postoperatively but is prohibitively high in patients receiving thrombolytic treatment or LMWHs. Careful consideration should be given to the timing of insertion and removal of the catheter. The risk of complications is similar whether the catheter is placed at the thoracic or lumbar level. Other complications include pruritus, nausea, urinary retention, and delayed respiratory depression. The latter is less than 1% when epidural morphine is used, similar to

Table 9.2 Epidural Opioid/Bupivacaine Combinations Administered by Continuous Infusion[a]

DRUG COMBINATIONS	SOLUTION[b]	BOLUS DOSE OF BUPIVACAINE	BASAL INFUSION[c]	BREAKTHROUGH DOSES	INCREMENTS IN BREAKTHROUGH[d]
Morphine	0.01%		6–8 mL/h	1–2 mL every 10–15 min	1 mL of the solution
Bupivacaine[e]	0.05%–0.1%	0.5%–0.25%			
Hydromorphone	0.0025%–0.005%		6–8 mL/h	1–3 mL every 10–15 min	1 mL of the solution
Bupivacaine[f]	0.05%–0.1%	0.5%–0.25%			
Fentanyl	0.001%		0.1–0.15 mL/kg/h	1–1.5 mL every 10–15 min	1 mL of the solution
Bupivacaine[g]	0.05%–0.1%	0.5%–0.25%			
Sufentanil	0.0001%		0.1–0.2 mL/kg/h	1–1.5 mL every 10–15 min	1 mL of the solution
Bupivacaine[h]	0.05%–0.1%	0.5%–0.25%			

[a] Catheter insertion site is the dermatome corresponding to the middle of the surgical incision. Administer a bolus dose of 0.5% bupivacaine or 2% lidocaine to establish surgical anesthesia, or 0.25% bupivacaine to induce postoperative analgesia in 5-mL aliquots.
[b] Due to infectious control, a total volume of 150 mL is recommended.
[c] Initial basal infusion rates will depend on the age, general condition, and weight of the patient.
[d] If analgesia is inadequate after 1 hour, increase the breakthrough dose by the recommended amount. If analgesia is inadequate after one additional hour, decrease the lockout interval by 5 minute.
[e] Prepare this solution by mixing 75–150 mg of bupivacaine with 15 mg of preservative-free morphine in a total volume of 150 mL of preservative-free normal saline.
[f] Prepare this solution by mixing 75–150 mg of bupivacaine with 3.75–7.5 mg of hydromorphone in a total volume of 150 mL of preservative-free normal saline.
[g] Prepare this solution by mixing 75–150 mg of bupivacaine with 1,500 μg of fentanyl in a total volume of 150 mL of preservative-free normal saline.
[h] Prepare this solution by mixing 75–150 mg of bupivacaine with 150–300 μg of sufentanil in a total volume of 150 mL of preservative-free normal saline.
From deLeon-Cosa Sola OA, Lema MJ: Postoperative epidural opioid analgesia: What are the choices? *Anesth Analg.* 1996;83:867–875, with permission.

the oral and parenteral route. Difficulty ambulating and orthostatic hypotension are minimized when catheters are placed in the thoracic region with low infusion rates and bupivacaine concentrations used are less than 0.08%.

Systemic narcotic analgesia can be used to provide effective postoperative pain control. Intravenous narcotics are commonly administered by a patient-controlled analgesia (PCA) pump after this type of procedure, allowing the patient to titrate the dose of narcotic to achieve adequate pain control. These modified infusion pumps are able to administer infusions of narcotics, small preprogrammed bolus doses on patient demand, and larger bolus doses by prescription. The PCA technique allows the patients to self-titrate narcotic doses to achieve optimal analgesic doses while avoiding the toxic side effects that result from high peak serum levels.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1487–1497.

DeLeon-Casa Sola OA, Lema MJ. Postoperative epidural opioid analgesia: what are the choices? *Anesth Analg*. 1996;83:867–875.

Liu S, Carpenter RL, Neal JM. Epidural anesthesia and analgesia. Their role in postoperative outcome. *Anesthesiology*. 1995;82:1474–1506.

Mann C, Pouzeratte Y, Boccara G, et al. Comparison of intravenous or epidural patient-controlled analgesia in the elderly after major abdominal surgery. *Anesthesiology*. 2000;92:433–441.

Yeager M, Glass DD, Neff RK, et al. Epidural anesthesia and analgesia in high-risk surgical patients. *Anesthesiology*. 1987;66:729–736.

CHAPTER 10

Hypertension

Manuel L. Fontes and Fun-Sun F. Yao

A 70-YEAR-OLD MAN

with cholelithiasis was scheduled for a cholecystectomy. His blood pressure (BP) was 230/120 mm Hg; pulse, 60 beats per minute. Hematocrit was 38%; serum sodium, 140 mEq per L; and serum potassium, 2.7 mEq per L. His medications included metoprolol, aspirin, atorvastatin (Lipitor), and hydrochlorothiazide.

A. Medical Disease and Differential Diagnosis

1. Define hypertension and classify its severity.
2. What is the prevalence of hypertension?
3. What is the general classification of hypertension? Enumerate the causes of each type of hypertension.
4. What are the clinical patterns of hypertension encountered?
5. What is the pathophysiology of essential hypertension?
6. What is the pathophysiology of isolated systolic hypertension (ISH) and of pulse pressure hypertension (PPH)?
7. What are the end-organ damages caused by long-standing hypertension?
8. Are hypertensive patients at an increased risk for perioperative cardiac morbidity?
9. Perioperative cerebral and renal complications are mostly associated with which subtype of hypertension?
10. Would you employ a controlled hypotensive technique for hypertensive patients? How much would you safely lower the BP?
11. What is the mechanism of action of antihypertensive drugs?
12. Does the choice of antihypertensive therapy influence hemodynamic responses to induction, laryngoscopy, and intubation?
13. Does chronic angiotensin-converting enzyme (ACE) inhibition influence anesthetic induction?

B. Preoperative Evaluation and Preparation

1. How would you evaluate this patient preoperatively?
2. Would you postpone the surgery? Why? What BP would you like the patient to achieve before surgery?
3. Should all or any of the chronic medications be discontinued before the operation?
4. Should hypokalemia be treated before anesthesia? Why?
5. Should hypomagnesemia be treated before anesthesia? Why?
6. Does an asymptomatic carotid bruit increase the risk in these patients?
7. The surgery was postponed for 6 weeks. The patient was on metoprolol, aspirin, atorvastatin, captopril, hydrochlorothiazide, and potassium chloride. His BP was 160/60 mm Hg and potassium 4.0 mEq per L. How would you premedicate this patient?
8. If the patient is an untreated hypertensive patient with BP 170/70 mm Hg, would you treat the patient preoperatively with an antihypertensive agent?

C. Intraoperative Management

1. How would you monitor this patient?
2. What are the anesthetic goals for hypertensive patients?
3. How would you induce anesthesia for the hypertensive patient?
4. How does tracheal intubation produce hypertension?
5. What happens to the left ventricular ejection fraction during and immediately following intubation?
6. What other measures can prevent hypertension and tachycardia at the time of intubation?
7. After induction and intubation, the BP decreased to 70/40 mm Hg. What would you do?
8. What is your choice of agents for maintenance of anesthesia? Why?
9. How would you manage fluid therapy for hypertensive patients?
10. During the surgery, BP increased to 220/120 mm Hg. How would you treat the hypertension?
11. What could you do to prevent hypertension during extubation and emergence?
12. Would you consider regional anesthesia for this patient?

D. Postoperative Management

1. The patient developed hypertension BP 210/110 mm Hg in the postanesthesia care unit. What would you do?

A. Medical Disease and Differential Diagnosis

A.1. Define hypertension and classify its severity.

True systemic hypertension can be diagnosed when there is an increase in arterial pressure above accepted normal pressure for age, sex, and race. According to the latest classification and characterization of BP by the Joint National Committee on Evaluation, Detection, and Prevention of High Blood Pressure, an optimal BP for adults is less than 120 mm Hg systolic with a diastolic of less than 80 mm Hg. Table 10.1 shows the categories of BP for optimal, normal, and high

Table 10.1 Categories of Blood Pressure and Subtypes of Hypertension

JNC 6 CATEGORY	SBP/DBP	JNC 7 CATEGORY
Optimal	<120/<80	Normal
Normal	120–129/80–84	Prehypertension
Borderline	130–139/85–89	
Hypertension	≥140/≥90	Hypertension
Stage 1	140–159/90–99	Stage 1
Stage 2	160–179/100–109	Stage 2
Stage 3	≥180/≥110	

DBP, diastolic blood pressure; JNC, Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; SBP, systolic blood pressure

Sources: The Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Arch Intern Med.* 1997;157:2413–2446.

The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *JAMA.* 2003;289:2560–2571.

normal as well as the two stages of hypertension. The accepted upper limits of normal BP in pediatric are as follows:

Adolescent	100/75 mm Hg
Early childhood	85/55 mm Hg
Infant	70/45 mm Hg

It is important to note that newer classification of hypertension define and specify hypertension according to systolic and to diastolic hypertension, each representing different pathophysiologic processes. Systolic hypertension is a marker of macrovascular disease and large arterial stiffening (atherosclerosis) and diastolic hypertension is a consequence of microvascular disease involving typically vessels less than 1 mm in size.

Hypertension is also categorized as urgent and emergent. According to the JNC VII Report, hypertensive emergency is defined as BP >180/120 mm Hg complicated by evidence of impending or progressive end-organ damage, whereas hypertensive urgency is severe elevation of BP without progressive end-organ damage.

Fauci AS, Braunwald E, Kasper DL, et al., eds. *Harrison's Principles of Internal Medicine.* 17th ed. New York: McGraw-Hill; 2008:1549–1562.

Joint National Committee on Prevention Detection, Evaluation, and Treatment of High Blood Pressure. The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *JAMA.* 2003:289.

Libby P, Bonow RO, Mann DL, et al., eds. *Braunwald's Heart Disease.* 8th ed. Philadelphia: WB Saunders; 2008:1027–1046.

A.2. What is the prevalence of hypertension?

The prevalence of hypertension depends on both the racial composition of the population and the criteria used to define hypertension. In a white suburban population like that in the Framingham study, nearly one-fifth have BP greater than 160/95 mm Hg,

and almost one-half have BP greater than 140/90 mm Hg. A higher prevalence has been found in the non-white population. The frequency increases with the age of the population with nearly two-thirds of hypertensive patients being older than 50 years. The subtype of hypertension is also influenced by age. Younger individuals suffer from diastolic hypertension and combined systolic and diastolic hypertension whereas older persons predominantly experience systolic hypertension. The number of hypertensive persons in the United States in 1983 was estimated to be 57.7 million—more than double the estimate made in 1960 to 1962. Currently, approximately 70 million Americans suffer from hypertension.

Aronson S, Fontes ML. Hypertension: a new look at an old problem. *Curr Opin Anesth.* 2006;19:59–64.

Fauci AS, Braunwald E, Kasper DL, et al., eds. *Harrison's Principles of Internal Medicine.* 17th ed. New York: McGraw-Hill; 2008:1549–1562.

Franklin SS, Larson MG, Khan SA, et al. Does the relation of blood pressure to coronary heart disease risk change with aging? The Framingham Heart Study. *Circulation.* 2001;1031:1245–1249.

Joint National Committee on Prevention Detection, Evaluation, and Treatment of High Blood Pressure. The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *JAMA.* 2003:289.

Libby P, Bonow RO, Mann DL, et al., eds. *Braunwald's Heart Disease.* 8th ed. Philadelphia: WB Saunders; 2008:1027–1046.

A.3. What is the general classification of hypertension? Enumerate the causes of each type of hypertension.

Hypertension is classified according to its subtypes: systolic, diastolic, and pulse pressure (Table 10.2). Historically, only diastolic hypertension—essential hypertension—was recognized, but more recently, there has been increasing emphasis and recognition of systolic hypertension, namely, *isolated systolic hypertension* (ISH). ISH is the most common subtype of hypertension affecting predominantly individuals older than 60 years of age. In fact, approximately 70% of hypertensive patients have ISH with approximately half of these individuals having very wide pulse pressure (>65 mm Hg) or *pulse pressure hypertension* (PPH). Isolated diastolic hypertension is most prevalent in individuals younger than 50 years and is an important marker of coronary heart disease and mortality in this age group. Some

Table 10.2 Classification of Hypertension

Systolic and diastolic hypertension
• Essential
• Renal
• Endocrine
• Neurogenic
• Miscellaneous
Systolic hypertension with wide pulse pressure
• Increased cardiac output
• Rigidity of aorta

hypertensive patients have both systolic and diastolic hypertension categorized as *combined systolic and diastolic hypertension*. The ranges of systolic, diastolic, and pulse pressure that define each subtype of hypertension are presented in Table 10.1.

Etiology of hypertension

- *Essential hypertension*. Unknown etiology
- *Renal*. Acute and chronic glomerulonephritis, chronic pyelonephritis, polycystic kidney, diabetic nephropathy, hydronephrosis, renovascular stenosis, renin-producing tumors, primary sodium retention
- *Endocrine*. Adrenal—Cushing syndrome, primary aldosteronism, congenital adrenal hyperplasia, pheochromocytoma, acromegaly, hypothyroidism, carcinoid, hyperthyroidism, oral contraceptives, corticosteroids
- *Neurogenic*. Psychogenic, increased intracranial pressure, spinal cord section, familial dysautonomia, lead poisoning, Guillain-Barré syndrome, sleep apnea
- *Miscellaneous*. Coarctation of aorta, increased intravascular volume, pregnancy-induced hypertension, polyarteritis nodosa, acute porphyria, hypercalcemia, alcohol and drug use, acute stress including surgery

Benetos A, Thomas F, Safar ME. Should diastolic and systolic blood pressure be considered for cardiovascular risk evaluation: a study in middle-aged men and women. *J Am Coll Cardiol*. 2001;37:163–168.

Fauci AS, Braunwald E, Kasper DL, et al., eds. *Harrison's Principles of Internal Medicine*. 17th ed. New York: McGraw-Hill; 2008:1549–1562.

Franklin SS, Khan SA, Wong ND, et al. Is pulse pressure useful in predicting risk for coronary heart disease? The Framingham Heart Study. *Circulation*. 1999;100:353–360.

Joint National Committee on Prevention Detection, Evaluation, and Treatment of High Blood Pressure. The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *JAMA*. 2003:289.

Kannel WB. Cardiovascular hazards of components of blood pressure. *J Hypertens*. 2002;20:395–397.

Libby P, Bonow RO, Mann DL, et al., eds. *Braunwald's Heart Disease*. 8th ed. Philadelphia: WB Saunders; 2008:1027–1046.

Sesso HD, Stampfer MJ, Rosner B, et al. Systolic and diastolic blood pressure, pulse pressure, and mean arterial pressure as predictors of cardiovascular disease risk in men. *Hypertension*. 2000;36:801–807.

A.4. What are the clinical patterns of hypertension encountered?

- "Vasoconstricted" hypertension—in medical patient with chronic renovascular hypertension, characterized by diastolic hypertension and systemic vascular resistant with normal or even decreased cardiac output and heart rate.
- "Hyperdynamic" hypertension—in postoperative surgical patient, characterized by acute systolic hypertension; widened pulse pressure; and increased cardiac output, heart rate, and systemic vascular resistant.

Joint National Committee on Prevention Detection, Evaluation, and Treatment of High Blood Pressure. The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *JAMA*. 2003:289.

Libby P, Bonow RO, Mann DL, et al., eds. *Braunwald's Heart Disease*. 8th ed. Philadelphia: WB Saunders; 2008:1027–1046.

Sladen RN. Perioperative hypertension. *IARS review course lectures*. Cleveland: International Anesthesia Research Society; 2002:100–114.

A.5. What is the pathophysiology of essential hypertension?

The underlying mechanism of essential hypertension is unknown. A variety of abnormalities, including heredity, fetal undernutrition, abnormal sympathetic nervous system activity, cell membrane defects, renal retention of excess salt, microcirculatory alterations, endothelial cell dysfunction, hyperinsulinemia secondary to insulin resistance, vascular hypertrophy, and altered renin–angiotensin system regulation are implicated. There is increasing evidence that "local renin–angiotensin" paracrine factors may be involved in the development of hypertension. However, characteristic hemodynamic changes are present as follows:

- Increased systemic vascular resistance with normal cardiac output
- Markedly increased sympathetic response to stress such as endotracheal intubation
- A greater increase in BP with vasoconstriction and a greater decrease in BP with vasodilation because of the increased thickening of arterial wall and high ratio of wall thickness to internal diameter

The higher the level of BP, the more likely that various cardiovascular diseases will develop prematurely through acceleration of arteriosclerosis. If untreated, approximately 50% of hypertensive patients die of coronary heart disease or congestive heart failure (CHF), approximately 33% of stroke, and 10% to 15% of renal failure.

Fauci AS, Braunwald E, Kasper DL, et al., eds. *Harrison's Principles of Internal Medicine*. 17th ed. New York: McGraw-Hill; 2008:1549–1562.

Libby P, Bonow RO, Mann DL, et al., eds. *Braunwald's Heart Disease*. 8th ed. Philadelphia: WB Saunders; 2008:1027–1046.

A.6. What is the pathophysiology of isolated systolic hypertension (ISH) and of pulse pressure hypertension (PPH)?

ISH is a manifestation of atherosclerotic disease involving predominantly the aorta and its major branches. Both ISH and PPH reflect arterial stiffening and represent the pulsatile component of BP, whereas the mean arterial pressure (MAP) represent the static state. Systole, then, is directly influenced by the ventricular contractile state, the ejected volume, heart rate, and, importantly, compliance of the aorta and pulse wave velocity. With increasing age and factors such as diabetes, smoking, increased cholesterol as well as some genetic factors, compliance of the aorta diminishes markedly (Fig. 10.1). The net result is stiffening of the arterial tree and inability to absorb the pulsatile load, causing the systolic pressure to rise sharply. Pulse wave velocity has gained much attention lately because it may be a richer substrate for characterizing the physiology of blood flow and pressure. Under normal physiologic conditions, the ejected blood volume is transmitted peripherally as a propagated wave. After reaching the periphery, in particular, at the bifurcation sites, a reflected wave or a retrograde wave is generated from the encountered impedance. Under normal conditions, wave reflection arrival coincides with the beginning of diastole, thereby augmenting the diastolic pressure. However, with stiffening of the aorta as occurs with aging, both the propagated and the reflected waves travel much more rapidly, and early return of the reflected arterial wave during late systole augments the systolic component, effectively increasing afterload. The ensuing loss of diastolic augmentation results in a disproportionate increase in the systolic blood pressure and lower diastolic blood pressure—a hallmark of ISH and of PPH.

Mechanistically, pulse pressure is also an index of the stiffness of conduit vessels and the rate of pressure wave propagation and reflection within the arterial tree. Approximately half of patients with ISH also have wide pulse pressure; however, both individuals who are normotensive (systolic, <140 mm Hg) with a low diastolic pressure

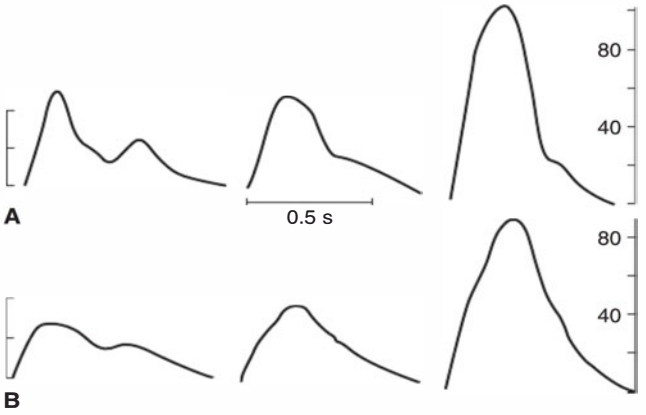

Figure 10.1 Change in amplitude and contour of the upper limb **(A)** and ascending aortic **(B)** pressure wave with age, as recorded in three female members of a family: at age 18 **(left)**, at age 48 **(center)**, and 97 years **(right)**. Upper limb pulse pressure was just more than twice as high in the old compared with the young subject (102 vs. 46 mm Hg), whereas aortic pulse pressure was more than three times higher (104 vs. 27 mm Hg). (From O'Rourke MF, Nichols WW. Aortic diameter, aortic stiffness, and wave reflection increase with age and isolated systolic hypertension. *Hypertension.* 2005;45(4):652–628, with permission.)

or persons with combined systolic and diastolic hypertension (systolic >140 mm Hg and diastolic >90 mm Hg) can have wide pulse pressure (normal values being ≤40 mm Hg).

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A.7. What are the end-organ damages caused by long-standing hypertension?

The end-organ damages caused by long-standing hypertension are as follows:

Cardiac involvement:
Left ventricular hypertrophy (LVH)
Angina or myocardial infarction (MI)

Arrhythmias
Congestive failure

Eye involvement:
Vascular changes in the fundus reflect hypertensive retinopathy and arteriosclerotic retinopathy

Renal involvement:
Nephropathy

Cerebral involvement:
Stroke or transient ischemic attack

Complications of hypertension to vascular disease probably involve three interrelated processes: pulsatile flow, endothelial cell dysfunction, and smooth muscle cell hypertrophy. These three interrelated processes are probably responsible for the arteriolar and arterial sclerosis that is the usual consequence of long-standing hypertension. Large vessels such as the aorta may be directly affected and be at risk for aneurysms and dissection. As discussed previously, the consequences of long-standing hypertension need be addressed according to the subtypes of hypertension; for the associated risks for cerebral, cardiac, and renal vascular complications differ according to systolic, diastolic, and PPH. For example, diastolic hypertension being a better predictor of coronary heart disease in younger patients, whereas systolic and pulse pressure being associated with greater risk of stroke, coronary heart disease and mortality in persons older than 60 years.

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A.8. Are hypertensive patients at an increased risk for perioperative cardiac morbidity?

Hypertensive patients are at increased risk for coronary artery disease, silent myocardial ischemia, CHF, and stroke. However, whether preoperative hypertension is predictive of perioperative major cardiac morbidity remains controversial. Some investigators have shown that patients with untreated, poorly controlled, or labile preoperative hypertension are at increased risk for perioperative BP lability, dysrhythmias, myocardial ischemia, and transient neurologic complications. Some suggested that preoperative hypertension predicted perioperative MI. However, Goldman and Caldera demonstrated that mild-to-moderate hypertension did not increase the risk of major morbid events. Instead, preoperative hypertension may predict several intermediates of outcome, such as BP lability and myocardial ischemia. The controversy may be due to the wide variability in the hypertensive population. Hypertension may affect perioperative morbidity through the extent of end-organ damage and not the manifestation of the disease itself. LVH, which signifies long-standing poorly controlled hypertension, can increase the risk of myocardial ischemia from imbalances of myocardial oxygen supply and demand regardless of the presence or absence of coronary artery disease.

ISH (systolic BP >140 mm Hg and diastolic BP <90 mm Hg) has been identified as a risk factor for cardiovascular complications in the general population and treatment reduces the future risk of stroke. More recently, Aronson and Fontes found that amongst the various component of BP, preoperative pulse pressure was independently and significantly associated with postoperative stroke, renal failure, and mortality in patients undergoing coronary artery bypass. Neither ISH nor isolated diastolic hypertension were predictive of vascular complications. This finding is consistent with results of longitudinal studies finding that increase in pulse pressure is a better predictor of major vascular complications than either systolic or diastolic BP. Interestingly, rises in pulse pressure as few as 10 mm Hg in both normotensive and hypertensive individuals is associated with 20% or more increase risk of renal, coronary, and cerebral events.

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A.9. Perioperative cerebral and renal complications are mostly associated with which subtype of hypertension?

Both systolic hypertension and high pulse pressure are strongly associated with risk for perioperative cerebrovascular accidents and acute renal failure. The brain and the kidneys as well as the heart differ from most organs in that they receive large amount of blood flow and have very low resistance. As such, the pulsatile load (pulse pressure) tends to be very high. Over a period of many years of poorly or untreated hypertension, endothelial injury and vascular remodeling changes can promote both arteriosclerosis and atherosclerosis, which are known risk factors for cerebral and renal vascular complications. The pulsatile stress also can cause dislodgment of plaques from the aorta and its major branches, resulting in embolic stroke.

In hypertensive patients, autoregulation of cerebral blood flow is reset to a higher range than normal, and although it protects the brain against sudden increases in

pressure, it makes it more vulnerable to hypotension. Therefore, when BP is lowered acutely, hypertensive patients will show signs of cerebral ischemia at a higher level of BP than normotensive patients.

Hypertension may accelerate cognitive decline with age. Hypertension, particularly systolic, is a major risk factor for initial and recurrent stroke and for transient ischemia attacks caused by extracranial atherosclerosis.

Chronic renal insufficiency is a common sequela of hypertension. Patients with hypertension should have a measurement of baseline serum creatinine. In the original Cardiac Risk Index, an elevated serum creatinine level (>3.0 mg per dL [>265.2 mmol per L]) was one of the independent risk factors for perioperative cardiovascular morbidity and mortality. This has been confirmed in the revised Cardiac Risk Index in which a preoperative serum creatinine level greater than 2.0 mg per dL (176.8 mmol per L) was one of six independent factors that predicted increased cardiovascular risk.

Aronson S, Fontes ML, Miao Y, et al., for the Investigators of the Multicenter Study of Perioperative Ischemia Research Group and the Ischemia Research and Education Foundation. Risk index for perioperative renal dysfunction/failure: Critical dependence on pulse pressure hypertension. *Circulation.* 2007;115(6):733–742.

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A.10. Would you employ a controlled hypotensive technique for hypertensive patients? How much would you safely lower the BP?

Uncontrolled or untreated severe hypertension is a contraindication to controlled hypotension. However, controlled hypotension may be used with caution in treated hypertensive patients. Because cerebral autoregulation is shifted to the right with chronic hypertension, the lower limit of controlled hypotension should be higher for hypertensive patients. However, with long-term treatment, the autoregulation curve shifts leftward to approach that in normals. Strangaard found that the lower limit of autoregulation was 113 mm Hg in severe untreated or uncontrolled hypertensives; 96 mm Hg in formerly severe, now-treated hypertensives; and 73 mm Hg in normotensive patients. The lowest level of mean BP tolerated without symptoms of hypoperfusion was 65 mm Hg in severe hypertensives, 53 mm Hg in treated hypertensives, and 43 mm Hg in normal patients. However, although the autoregulation may shift toward normal with treatment, in many patients the autoregulation did not shift toward normal even after 12 months of treatment. Because one cannot measure patients' autoregulation, a useful clinical guide is that a 25% decrease in MAP reaches the lower limit of autoregulation and a 55% decrease in MAP reaches symptomatic cerebral hypoperfusion. Another suggested rule is that the systolic pressure of controlled hypotension should not be lower than the diastolic pressure of the patient's usual pressure. It is important to note that peripherally measured blood pressure do

not match central aorta blood pressure, which is more reflective of actual cerebral blood pressure.

Recently, noninvasive cerebral oximeter using near-infrared spectroscopy may be used to monitor the oxygen saturations of cerebral cortex. The values of cerebral oxygen saturations correspond with those of a mixture of 85% jugular venous O_2 saturation and 15% of arterial O_2 saturation. It reflects the balance between cerebral O_2 delivery and O_2 demand. In a steady state of anesthesia, the cerebral O_2 demand does not change significantly. Therefore, cerebral O_2 saturations will not decrease until the BP falls below its autoregulation range. Therefore, the cerebral oximeter may be employed to determine the lower limit of autoregulation and to ensure adequate cerebral oxygenation. Unfortunately, there is wide variability in measured cerebral saturations with some individual's baseline oximetric saturation values being near 50% at baseline. Further, the measured value is reflective of regional saturation such that distant areas that may be ischemic are not detected.

It should be mentioned that neither the threshold for upper nor lower limits of systolic and diastolic BP have been established. Frequently, these limits have been chosen arbitrarily and the relation of perioperative hypertension to outcomes has been inconsistent among the studies that have addressed this question. In part, the limitation comes from grouping all types of hypertension together. Moreover, available vasoactive agents are not selective in lowering or raising systolic BP and diastolic BP without a concomitant increase or fall in the other component. Undermining the broad-based reliance on systolic BP and diastolic BP are a number of studies in humans over the past several decades that clearly show that both morbidity and mortality do not always linearly correlate with rises or fall in BP. In individuals with demonstrable coronary disease, namely, those with previous infarcts, coronary mortality was significantly related to diastolic pressure in a U-shape configuration—occurring more frequently in those with very high or very low diastolic BP. Unfortunately, the emphasis on BP management perioperatively has been to control the systolic component with no attention paid to the diastolic component. This is particularly concerning in patients with ISH and with very wide pulse pressure where the diastolic BP is already critically low. By reducing the systolic component, further lowering of the diastolic BP can result in ischemic complications in most sensitive vascular beds such as the brain, the heart, and the kidneys. Lastly, it is critical to recognize that peripheral arterial pressures do not necessarily reflect central pressures with exception of the MAP. In a subset of hypertensive individuals, both the systolic and the pulse pressures are grossly higher peripherally as compared to central aortic pressures, such that lowering of the peripheral BP may result in critical reduction in perfusion pressure.

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A.11. What is the mechanism of action of antihypertensive drugs?

Antihypertensive drugs are categorized by their mechanism of action as follows.

Diuretics

They include thiazides (e.g., hydrochlorothiazide), loop diuretics (e.g., furosemide, ethacrynic acid), and potassium-sparing agents (e.g., spironolactone, triamterene). All diuretics initially lower the BP by increasing urinary sodium excretion and by reducing plasma volume, extracellular fluid volume, and cardiac output. Within 6 to 8 weeks, the cardiac output returned to normal. The lowered BP is related to a fall in peripheral resistance. Diuretics may cause hypokalemia, hypomagnesemia, hyperuricemia, hyperlipidemia, hypercalcemia, and hyperglycemia. For patients with ST-segment changes and evidence of pulmonary edema and hypertension or with increased intracranial cerebral pressure and hypertension, intravenous furosemide may be appropriate.

Antiadrenergic agents

- *Centrally acting drugs*. Clonidine, dexmedetomidine, and mivazerol. These drugs and their metabolites are primarily α_2-receptor agonists. Stimulation of α_2 receptors in the vasomotor centers of the brain reduces sympathetic outflow.
- *Peripherally acting drugs*
  - α-Receptor blockers
    α_1 and α_2 Receptors—phenoxybenzamine (Dibenzyline), phentolamine (Regitine)
    α_1 Receptor—prazosin (Minipress), doxazosin (Cardura)
    By blocking α-mediated vasoconstriction, these drugs induce a fall in peripheral resistance with both arteriolar and venous dilation.
  - β-Receptor blockers—atenolol (Tenormin), metoprolol (Lopressor), nadol (Corgard), pindolol (Visken), propranolol (Inderal), esmolol (Brevibloc). These drugs lower the BP by decreasing heart rate, contractility, cardiac output, and renin levels. BP is decreased without reflex tachycardia or widening of the pulse pressure. They also have antiarrhythmic activity and suppress both ventricular and supraventricular ectopic rhythms.
  - α- and β-Receptor blockers—labetalol (Trandate)
  - Endothelin receptor antagonist—act on endothelin A and B receptors to block the effect of endothelin-1, which is the most potent vasoconstrictor that is secreted primarily from vascular smooth muscle and endothelial cells. Bosentan (receptor A and B antagonist) and sitaxsentan (receptor A antagonist) are examples of a few of this class of agents used in the management of pulmonary hypertension and less so for hypertension-related heart failure

Direct vasodilators

They include hydralazine, nitroprusside, nitroglycerin, and calcium channel blockers. These drugs directly relax the smooth muscle of resistance and capacitance vessels to different degrees.

Dopaminergic agonists

Dopaminergic agonists (DAs) are classified into DA_1 and DA_2 subtypes.

Stimulation of DA_1 receptors causes vasodilation, and inhibition of active sodium transport in the proximal tubule, leading to natriuresis.

Stimulation of DA_2 receptors inhibits norepinephrine release and promotes peripheral vasodilation.

Fenoldopam, a dopamine receptor (DA_1 selective) agonist and a systemic and renal vasodilator, offers significant advantages as a parenterally administered agent for the management of BP in hypertensive emergencies and in the periop-

Table 10.3 Cardiovascular Effects of Calcium Channel Blockers

	VERAPAMIL	DILTIAZEM	NIFEDIPINE	NICARDIPINE	CLEVIDIPINE
Heart Rate	⇓	⇓	⇑ or -	⇑ or -	-
Nodal Conduction	⇓⇓	⇓	⇓ or -	-	-
Myocardial Depression	⇑⇑	⇑	-	-	-
Vasodilation	⇑	⇑	⇑⇑	⇑⇑	⇑⇑

↑↑, more increase; ↓↓, more decrease; ↑, increase; ↓, decrease; –, no change.

erative setting. Parenteral fenoldopam has a rapid onset and offset of effect, with an elimination half-time of approximately 10 minutes. Prepared in concentration of 10 mg in 250 mL (40 μg/mL), the recommended starting dose is 0.05 μg/kg/minute. This should be titrated to effect by 0.025 μg/kg/minute every 10 to 15 minutes, to a maximum dose of 0.5 to 0.8 μg/kg/minute. The drug should not be administered in boluses; the incidence of reflex tachycardia is related to rapidity of upward titration. Unlike dopamine, it has no β- or α-adrenergic activity and increasing doses result in increasing vasodilation without tachycardia or tachyarrhythmias.

Calcium channel blockers

The cardiovascular effects of calcium antagonists are listed in Table 10.3. These drugs decrease BP mainly by peripheral vasodilation. Renin and aldosterone secretion may be reduced as well.

Angiotensin-converting enzyme inhibitors

They include captopril, enalapril, lisinopril, quinapril, and ramipril. The renin–angiotensin system may be inhibited in four ways as shown in Figure 10.2. These drugs inhibit the conversion of the inactive decapeptide angiotensin I to the active octapeptide angiotensin II. Lower levels of angiotensin II may decrease BP by

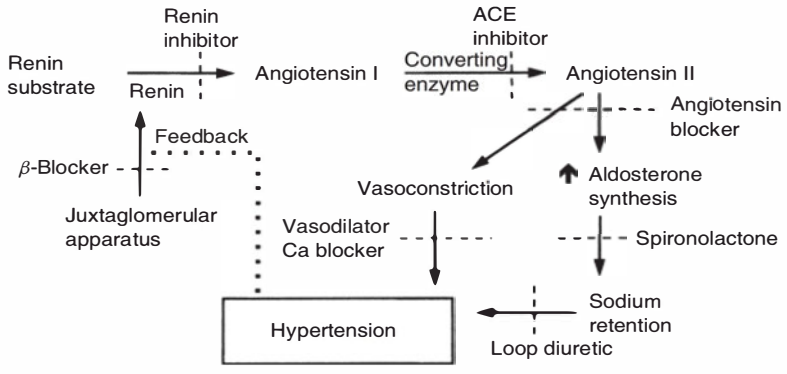

Figure 10.2 The renin–angiotensin system and the mechanism of action of antihypertensive drugs. ACE, angiotensin-converting enzyme.

reducing angiotensin II–induced vasoconstriction and by decreasing aldosterone synthesis. Angiotensin-converting enzyme (ACE) inhibitors also retard the degradation of a potent vasodilator (bradykinin), alter prostaglandin production (most notably with captopril), and can modify the activity of the adrenergic nervous system.

ACE inhibitors provide predominantly arterial vasodilation and have become primary therapy for the treatment of CHF by afterload reduction. Cardiac output is increased without excessive decrease in preload, with a favorable effect on survival.

Angiotensin II receptor blockers

Angiotensin II receptor antagonists or blockers (ARBs), represent the third class that antagonizes the renin–angiotensin–aldosterone system. Blockade of the action of angiotensin II leads to elevations in plasma levels of renin, angiotensin I, and angiotensin II. However, this build-up of precursors does not overwhelm the receptor blockade, as evidenced by a persistent fall in both BP and plasma aldosterone levels. There are several possible differences between ACE inhibitors and angiotensin II receptor antagonists. These include the following:

- ACE is a kininase. Therefore, inhibiting this enzyme, which normally degrades bradykinin, with an ACE inhibitor leads to increased kinin levels, an effect not seen with an angiotensin II receptor antagonist. High bradykinin levels may also provide additional vasodilation and other benefits not observed with angiotensin II receptor antagonists.
- ACE inhibitors, by decreasing angiotensin II production, reduce the effect of both AT_1 and AT_2 receptors; only the former are inhibited by the angiotensin II receptor blockers. Chronic stimulation of the AT_2 receptor may be beneficial.
- In the heart, kidney, and perhaps the blood vessels, the production of angiotensin II may be catalyzed by enzymes other than ACE, such as chymase. The effect of the angiotensin II produced by this reaction can be inhibited by the angiotensin II receptor antagonists but not by ACE inhibitors.

There is evidence that ARBs are more effective in treating ISH and PPH particularly in combination with ACE inhibitors and with endothelin receptor blockers.

Other vasodilators

They include brain natriuretic peptides such as nesiritide that is primarily used in acute exacerbation of heart failure to improve forward flow and reduce symptoms and signs of heart failure. There has been recent controversy about the clinical efficacy of these agents. Importantly, there have been several reports suggesting that the renal outcome is worsened in patients receiving nisiritide.

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A.12. Does the choice of antihypertensive therapy influence hemodynamic responses to induction, laryngoscopy, and intubation?

The pressor responses to induction, laryngoscopy, and intubation differ little whether patients with mild-to-moderate hypertension receive a β-blocker, a calcium channel blocker, an ACE inhibitor, or a diuretic. Even changes of a similar magnitude are also observed in untreated hypertensive patients. On the other hand, hypotensive responses may be magnified in those patients with poorly controlled hypertension following induction—generally due to a reduced intravascular volume in the face of increased vascular sympathetic tone. As mentioned previously, attention should be directed not only to the systolic but also to pulse and diastolic pressures.

Sear JW, Jewkes C, Teller JC, et al. Does the choice of antihypertensive therapy influence haemodynamic responses to induction, laryngoscopy and intubation? *Br J Anaesth*. 1994;73:303–308.

A.13. Does chronic angiotensin-converting enzyme (ACE) inhibition influence anesthetic induction?

Coriat et al. reported that, in hypertensive patients chronically treated with ACE inhibitors, therapy until the day of surgery is a major factor influencing BP responsiveness to anesthetic induction for vascular surgery. If enalapril (a long-acting ACE inhibitor) treatment is continued, a very low plasma-converting enzyme activity will be observed and an exaggerated hypotensive response may occur at induction. If captopril (a short-acting ACE inhibitor) treatment is continued, the magnitude of the decrease in BP in response to induction, although lower than with enalapril, is enhanced compared with that noted in patients in whom captopril had been stopped. All of the hypotensive episodes in patients who received ACE inhibitors until the day of surgery were easily corrected by administration of an α-agonist. The temporary withdrawal of these two ACE inhibitors attenuated the hypotensive response to induction but did not lead to an abnormal BP response to induction and intubation. However, recently, Ryckwaert and Colson reported that ACE inhibitor treatment in patients with infarction-induced myocardial dysfunction does not increase the incidence of severe hypotension after induction of anesthesia. In all, the overwhelming opinion is to continue all antihypertensive medication including the day of surgery and resumption of such therapy postoperatively. A number of studies have shown an improvement in outcome when therapy is continued versus a worsening in outcome when either ACE inhibitors or β-blockers have been withdrawn.

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B. Preoperative Evaluation and Preparation

B.1. How would you evaluate this patient preoperatively?

In addition to the routine systemic preoperative physical and history, special attention should be paid to the following: etiology and severity of hypertension, the subtype of hypertension, current therapy, and the end-organ damage from chronic hypertension.

The underlying cause of hypertension should be clear. Surgical mortality is relatively high in patients with renovascular hypertension. Moreover, failure to diagnose a pheochromocytoma preoperatively, albeit a rare finding, may prove fatal, because anesthetic agents are well known to precipitate a crisis in such patients. Meanwhile, the severity of hypertension alters anesthetic risk.

Antihypertensive drugs have different anesthetic implications. Diuretics frequently cause chronic hypokalemia and hypomagnesemia, which may increase the risk of arrhythmia. Therefore, serum electrolytes should be checked preoperatively.

The presence of target-organ damage in the brain, heart, and kidney signifies long-standing, poorly controlled hypertension. Unfortunately, markers of organ damage become demonstrable only after significant end-organ damage has occurred.

For cardiac evaluation, electrocardiogram and chest x-ray film serve as minimal tests. The echocardiogram will be helpful. LVH can increase the risk of perioperative myocardial ischemia from imbalances of myocardial oxygen supply and demand regardless of the presence or absence of coronary artery disease. There is a very high correlation between LVH, ISH and PPH—it is uncertain which comes first. Some authorities believe that hypertensive patients without evidence of LVH or other risk factors are at a lower perioperative cardiac risk and do not require further evaluation for most operations. Patients with severe hypertension are also at an increased risk for diastolic dysfunction causing CHF.

For renal evaluation, urinalysis, serum creatinine, and blood urea nitrogen should be measured to define the presence and extent of renal parenchymal disease. If chronic renal failure exists, hyperkalemia and elevated plasma volume may be of concern. Normal saline crystalloid intravenous solution is recommended for such cases.

For cerebrovascular evaluation, a history of cerebrovascular accidents and transient ischemic attacks and the presence of hypertensive retinopathy should be looked for.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:283.

Fleisher LA. Preoperative evaluation of the patient with hypertension. *JAMA*. 2002;287: 2043–2046.

Fleisher LA, Barash PH. Preoperative cardiac evaluation for noncardiac surgery. *Anesth Analg*. 1992;74:586–598.

B.2. Would you postpone the surgery? Why? What BP would you like the patient to achieve before surgery?

It is prudent to postpone elective surgery with a BP of 230/120 mm Hg. This patient should be considered to have hypertensive emergency if additional end-organ sequelae are present, in which case he needs to be admitted for intravenous control of BP. Otherwise, for hypertensive urgency, it is recommended that the patent be placed in a quiet environment and managed with rest and oral antihypertensives. The patient should be discharged and instructed to follow-up with his/her internist for management and control of hypertension. Prior to rescheduling for surgery., if time permits, the BP should be gradually lowered over 6 to 8 weeks to less than 140/90 mm Hg. Acute control within several hours is inadvisable before elective surgery because this practice may put the cerebral or other circulations at risk for ischemia.

In moderate hypertensive patients with severe end-organ involvement, preoperative BP should be normalized as much as possible, although in asymptomatic patients with mild-to-moderate hypertension (diastolic BP $<$110 mm Hg), elective surgery may proceed without increased cardiovascular risks. Goldman et al. found that patients with mild and moderate hypertension were not at increased risk of vascular complications unless they had other risks of coronary heart disease. In all, the thresholds being recommended apply only in part to today's surgical population. Most hypertensive patients presenting for surgery are elderly patients who suffer almost exclusively from ISH and PPH. It is uncertain what acute changes in BP preoperatively will have on outcome giving that the pathologic changes are chronic and unlikely to normalize with treatment. In patients with medically refractory coronary disease requiring coronary artery bypass grafting (CABG) surgery, PPH was associated with an increased risk of major vascular complication.

Fleisher LA. Preoperative evaluation of the patient with hypertension. *JAMA*. 2002;287: 2043–2046.

Fleisher LA, Barash PH. Preoperative cardiac evaluation for noncardiac surgery. *Anesth Analg*. 1992;74:586–598.

Fontes ML. New insights in hypertension. *ASA Refresher Courses Anesthesiol*. 2006;34:43–53.

Fontes ML, Aronson S, Mathew JP, et al., for the Multicenter Study of Perioperative Ischemia *(McSPI)* Research Group and the Ischemia Research and Education Foundation (IREF) Investigators. Risk of adverse outcome in coronary bypass surgery. *Anesth Analg*. 2008;107:1123–1130.

Gibney EM, Casebeer AW, Schooley LM, et al. Cardiovascular medication use after coronary bypass surgery in patients with renal dysfunction: a national Veterans Administration study. *Kidney Int*. 2005;68:826–832.

Nikolov N, Fontes M, White WD, et al. Is increased pulse pressure associated with a reduction in long-term survival after CABG surgery? *Anesth Analg*. 2010;110:335–40.

B.3. Should all or any of the chronic medications be discontinued before the operation?

Current opinion generally favors continuation of antihypertensive medications, especially β-blockers, up to the time of surgery. There is concern that acute withdrawal of these medications may precipitate ischemic myocardial events. Because β-blockade does not impair the hemodynamic response to hemorrhage and does not adversely affect responses to hypoxia, the medications should be continued. The withdrawal syndrome is characterized by an enhanced sensitivity to sympathetic stimulation and has been attributed to various factors, including sympathetic overactivity and increased triiodothyronine levels, but most probably it is a result of increased β-receptor density.

The safety of β-blockers and their benefits (prevention of hypertensive responses, dysrhythmias, and myocardial ischemia) have been long established. Similarly, treatment with calcium channel blockers, ACE inhibitors, statins, and diuretics can be maintained. Indeed, the responses to induction of anesthesia, laryngoscopy, and intubation differ little whether patients receive a β-blocker, a calcium channel blocker, an ACE inhibitor, or a diuretic. Withdrawal of clonidine has been associated with rebound hypertension.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1117.

Coriat P, Richters C, Douraki T, et al. Influence of chronic angiotensin-converting enzyme inhibition on anesthetic induction. *Anesthesiology*. 1994;81:299–307.

Fleisher LA. Preoperative evaluation of the patient with hypertension. *JAMA*. 2002;287: 2043–2046.

Pigott DW, Nagle C, Allman K, et al. Effect of omitting regular ACE inhibitor medication before cardiac surgery on haemodynamic variables and vasoactive drug requirements. *Br J Anaesth*. 1999;83:715–720.

Prichard BN, Walder RJ. The syndrome associated with the withdrawal of beta-adrenergic receptor blocking drugs. *Br J Clin Pharmacol*. 1982;13(suppl 2):337S–343S.

Sear JW, Jewkes C, Tellez JC, et al. Does the choice of antihypertensive therapy influence haemodynamic responses to induction, laryngoscopy and intubation? *Br J Anaesth*. 1994;73:303–308.

B.4. Should hypokalemia be treated before anesthesia? Why?

Hypokalemia is a frequent finding in hypertensive patients treated with the diuretic thiazides. It is important to maintain normal electrolyte balance in patients with heart or coronary artery disease. A low value of potassium (3.0 to 3.5 mEq per L) in these patients may cause arrhythmias, increase sensitivity to digitalis, and depress neuromuscular function. In patients without risk of cardiac complications of surgery and anesthesia, this modest reduction (3.0 to 3.5 mEq per L) should not prompt postponement of surgery or immediate potassium replacement. Patients with more severe potassium depletion (≤2.9 mEq per L) should be treated and/or undergo work-up for such profound hypokalemia. For those patients, at least 1 week before surgery supplemental potassium should be given if renal function is not impaired. In surgical emergencies, potassium may be given at a rate not to exceed 0.5 mEq per kg of body weight per hour. Administration should be stopped during surgery and restarted postoperatively, depending on serial potassium determinations. Vitez et al. concluded that chronic hypokalemia per se is not associated with a higher incidence of intraoperative arrhythmia.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:311–313.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone; 2008:334–355.

McGovern B. Hypokalemia and cardiac arrhythmias. *Anesthesiology*. 1985;63:127.

Vitez TS, Soper LE, Wong KC, et al. Chronic hypokalemia and intraoperative dysrhythmias. *Anesthesiology*. 1985;63:130–133.

B.5. Should hypomagnesemia be treated before anesthesia? Why?

The normal level of magnesium is between 1.5 and 2.5 mEq per L. Magnesium ion is essential for the proper function of most enzyme systems. Depletion is characterized by neuromuscular and central nervous system hyperexcitability. These signs are similar to those of calcium deficiency. Cardiovascular abnormalities include coronary artery spasm, cardiac failure, and dysrhythmias. When severe, hypomagnesemia may induce seizures, confusion, and coma. Replacement should be done only in cases of severe depletion. Magnesium should not be given to the oliguric patient and should be given very carefully to patients with renal insufficiency. Small intravenous doses should be used, with careful observation for toxicity (lethargy, weakness, and loss of deep tendon reflexes).

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:321–322.

B.6. Does an asymptomatic carotid bruit increase the risk in these patients?

Yes. The incidence of stroke is increased in such patients, although the stroke may not be thrombotic or related to the carotid artery in which the bruit was heard. Bruits are general predictors of vascular disease and may be predictors of perioperative strokes. It is important to note that in patients who are asymptomatic from their carotid stenosis, endarterectomy is no longer recommended. Nevertheless, there continues to be much debate on this topic.

De Feo M, Renzulli A, Onorati F, et al. The risk of stroke following CABG: one possible strategy to reduce it. *Int J Cardiol*. 2005;98(2):261–266.

Wolf P, Kannel WB, Sorlie P, et al. Asymptomatic carotid bruit and the risk of stroke: the Framingham study. *JAMA*. 1981;245:1442.

Yatsu FM, Hart RG. Asymptomatic carotid bruit and stenosis: a reappraisal. *Curr Concepts Cerebrovascular Dis*. 1982;17:21.

B.7. The surgery was postponed for 6 weeks. The patient was on metoprolol, aspirin, atorvastatin, captopril, hydrochlorothiazide, and potassium chloride. His BP was 160/60 mm Hg and potassium 4.0 mEq per L. How would you premedicate this patient?

Because half or more of hypertensive patients still have elevated BP despite treatment, the anesthesiologist should determine the anxiety level of the patient. With this knowledge, the premedication with diazepam, lorazepam, or midazolam can be regulated to have the patient arrive in the operating room sedated. However, due to a high occurrence of delirium in the elderly receiving benzodiazepines, premedication with such agents is being discouraged. This will help to prevent a starting BP well above the optimal level. All the antihypertensive medications are continued up to the day of surgery.

Cavaliere F, D'Ambrosio F, Volpe C, et al. Postoperative delirium. *Current Drug Targets*. 2005;6(7):807–814.

Lepouse C, Lautner CA, Liu L, et al. Emergence delirium in adults in the post-anaesthesia care unit. *Br J Anaesth*. 2006;96(6):747–753.

Wallace AW, Galindez D, Salahieh A, et al. Effect of clonidine on cardiovascular morbidity and mortality after noncardiac surgery. *Anesthesiology*. 2004;101(2):284–293.

B.8. If the patient is an untreated hypertensive patient with BP 170/70 mm Hg, would you treat the patient preoperatively with an antihypertensive agent?

Yes. The preoperative administration of clonidine, β-blockers, or angiotensin-converting enzyme (ACE) inhibitors has been advocated to reduce the intraoperative hemodynamic lability and myocardial ischemia in hypertensive patients. Clonidine, a central α_2 agonist, decreases sympathetic outflow and reduces plasma catecholamines, aldosterone levels, and renin activity. A single dose of clonidine, 5 μg per kg orally, 2 hours before surgery significantly decreases anesthetic requirements and hemodynamic lability in patients with mild-to-moderate hypertension. However, preoperative clonidine did not decrease BP lability during aortic operation. Perioperative use of clonidine also has been shown to have short and long-term benefits related to cardiac morbidity and survival.

The best treatment may be cardioselective β-blocker therapy. A single small oral dose of a β-adrenergic blocking agent such as labetalol, atenolol, or lopressor given preoperatively to untreated, asymptomatic, mildly hypertensive patients effectively attenuated tachycardia with tracheal intubation and emergence. The incidence of myocardial ischemia was reduced from 28% in the control group to 2% in the β-blocker groups. An oral-dose ACE inhibitor such as enalapril given preoperatively also attenuates the hemodynamic responses to intubation and surgical stimulation.

Engelman E, Lipszyc M, Gilbart E. Effects of clonidine on anesthetic drug requirements and hemodynamic response during aortic surgery. *Anesthesiology*. 1989;71:178–187.

Fleisher LA. Preoperative evaluation of the patient with hypertension. *JAMA*. 2002;287:2043–2046.

Ghignone M, Calvillo O, Quintin L. Anesthesia and hypertension: the effect of clonidine on perioperative hemodynamics and isoflurane requirements. *Anesthesiology*. 1987;67:3–10.

Stone JG, Foex P, Sear JW, et al. Myocardial ischemia in untreated hypertensive patients: effect of a single small oral dose of a beta-adrenergic blocking agent. *Anesthesiology*. 1988;68:495–500.

Wallace AW, Galindez D, Salahieh A, et al. Effect of clonidine on cardiovascular morbidity and mortality after noncardiac surgery. *Anesthesiology*. 2004;101(2):284–293.

Yeates AP. Anaesthesia and angiotensin-converting enzyme inhibitors. *Anaesthesia*. 1988;43:935–939.

C. Intraoperative Management

C.1. How would you monitor this patient?

- *Electrocardiogram*. Simultaneous leads V_5 and II, multiple lead ST analysis, if possible, are essential because hypertensive patients are at increased risk for myocardial ischemia regardless of the presence or absence of coronary disease.

- *BP*. A continuous monitoring of BP is essential because of lability of BP in these patients. Direct intra-arterial measurement of BP permits beat-to-beat observation. However, noninvasive automatic oscillometric techniques usually are sufficient.
- *Pulmonary artery catheter (PAC)*. Only for those hypertensive patients with a history of CHF or a recent MI, a PAC may be helpful in managing fluid replacement and monitoring ventricular function. Of note, there is a strong correlation between hypertension and LVH, which results in poor ventricular compliance reflected by elevated pulmonary artery occlusion pressure in the face of low or normal ventricular volumes and normal contractility. Presence of CHF in hypertensive patients is frequently a marker of diastolic dysfunction and NOT systolic dysfunction.
- *Pulse oximeter*. This should be used to monitor peripheral blood flow and oxygenation.
- *End-tidal CO_2 analyzer*. This monitor will help maintain normocarbia.

C.2. What are the anesthetic goals for hypertensive patients?

The anesthetic goal is to minimize wide lability of BP in response to anesthetic and surgical stimuli to prevent the following:

- Myocardial ischemia from tachycardia or less common from either hypertension or hypotension
- Cerebral hypoperfusion from hypotension
- Cerebral hemorrhage and hypertensive encephalopathy resulting from hypertension or embolic stroke from rupture of plagues either locally or from the aorta and the neck vessels.
- Renal failure from renal hypoperfusion

Particular attention to diastolic BP is strongly recommended while attempting to reduce systolic BP. It is unfortunate that clinical practice perioperatively hinges on manipulation of the systolic BP without attention to the diastolic component. This is particularly troublesome in most elderly patients who suffer from ISH and/or wide pulse pressure. In both subtypes of hypertension, the already lower diastolic pressure can easily be reduced further—predisposing to myocardial hypoperfusion and ischemia.

Recently, Lee et al. showed that patients with wide pulse pressure have an increased risk for thrombogenesis marked by elevated levels of D-dimers, von Willebrand factor, and platelet activation. This along with extensive atherosclerotic disease of the aorta, carotid, and renal arteries, which is also common in patients with ISH, provides a pathophysiologic basis for the increase incidence of perioperative stroke, MI, and renal dysfunction observed in hypertensive patients.

Lastly, careful control of the hemodynamic responses to noxious stimuli such as endotracheal intubation, surgical incision and manipulation, and emergence from anesthesia is essential in the hypertensive patient.

Fontes ML, Aronson S, Mathew JP, et al., for the Multicenter Study of Perioperative Ischemia *(McSPI)* Research Group and the Ischemia Research and Education Foundation (IREF) Investigators. Risk of adverse outcome in coronary bypass surgery. *Anesth Analg.* 2008;107:1123–1130.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease.* 5th ed. Philadelphia: Churchill Livingstone; 2008: 94–97.

Lee KW, Blann AD, Lip GY. High pulse pressure and nondipping circadian blood pressure in patients with coronary artery disease: relationship to thrombogenesis and endothelial damage/dysfunction. *Am J Health.* 2005;18:104–115.

Lovett JK, Howard SC, Rothwell PM. Pulse pressure is independently associated with carotid plaque ulceration. *J Hypertens.* 2003;21:1669–1676.

C.3. How would you induce anesthesia for the hypertensive patient?

While the patient is being preoxygenated, fentanyl, 7 to 8 μg per kg, is given slowly to achieve drowsiness. Then, either thiopental in 50-mg increments or propofol in 30 to 50 mg increments is titrated to produce unconsciousness, followed by succinylcholine, 1 mg per kg, or nondepolarizing muscle relaxants to facilitate tracheal intubation.

All anesthetic agents are acceptable with the possible exception of ketamine, which may produce significant hypertension and tachycardia. However, deeper anesthesia with potent inhalation agents to attenuate tachycardia and hypertension should be done with caution because of higher incidence of hypotension arising from both vasodilation and cardiac depression.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease.* 5th ed. Philadelphia: Churchill Livingstone; 2008:96.

Martin DE, Rosenberg H, Aukburg SJ, et al. Low-dose fentanyl blunts circulatory responses to tracheal intubation. *Anesth Analg.* 1982;61:680.

C.4. How does tracheal intubation produce hypertension?

Translaryngeal intubation of the trachea stimulates laryngeal and tracheal receptors, resulting in marked increase in the elaboration of sympathomimetic amines. This sympathetic stimulation results in tachycardia and a rise in BP. In normotensive patients, this rise is approximately 20 to 25 mm Hg; it is much greater in hypertensive patients. This increase in BP results from vasoconstriction, because of unopposed α stimulation in hypertensive patients taking β-blocking drugs.

Prys-Roberts C, Greene LT, Meloche R, et al. Studies of anaesthesia in relation to hypertension. II: haemodynamic consequences of induction and endotracheal intubation. *Br J Anaesth.* 1971;43:531.

C.5. What happens to the left ventricular ejection fraction during and immediately following intubation?

During and immediately following intubation associated with tachycardia and hypertension, there is a decrease in the left ventricular ejection fraction. This is particularly marked in patients with coronary artery disease. Nevertheless, such hemodynamic perturbations can be anticipated and treated accordingly with β-blockade, narcotic, and titration of hypnotic and/or inhalation agents.

Giles RW, Berger JH, Barash PG, et al. Continuous monitoring of left ventricular performance with the computerized nuclear probe during laryngoscopy and intubation before coronary artery bypass surgery. *Am J Cardiol.* 1982;50:735.

C.6. What other measures can prevent hypertension and tachycardia at the time of intubation?

The rise in BP and heart rate occurs approximately 14 seconds after the start of laryngoscopy and becomes maximal after 30 to 45 seconds of direct laryngoscopy. If possible, laryngoscopy time should be 15 seconds or less to minimize BP elevation. Simultaneous administration of fentanyl, 7 to 8 μg per kg with the induction dose of

thiopental or propofol, can blunt the cardiovascular response to tracheal intubation. Other measures are described as follows:

- Lidocaine, 1.5 mg per kg is given 2 minutes before intubation.
- Esmolol, up to 2 mg per kg, appears to be especially effective in providing consistent and reliable protection against hypertension and tachycardia with intubation. It is easy to titrate and does not exacerbate postintubation hypotension because of its short duration of action.
- Labetalol, 0.15 to 0.45 mg per kg is comparable to esmolol 1.5 to 4.5 mg per kg in attenuating hemodynamic effects. However, the half-lives of intravenous esmolol and labetalol are 9 minutes and 5 hours, respectively. Additionally, labetalol has minimal effects on heart rate and through its action on α receptors, it acts similar to a vasodilator, particularly with chronic use.
- Nicardipine, 1 mg intravenously 2 minutes before tracheal intubation maintained hemodynamic stability during the intraoperative period. Both doses of 0.015 and 0.03 mg per kg attenuated BP but not heart rate responses during emergence and extubation. Greater BP control occurred with the larger nicardipine dose of 0.03 mg per kg.

It is important to remember that all the previously mentioned doses are used with a single agent only. If a combination of different agents or anesthetics is used, doses should be decreased accordingly. Otherwise, severe hypotension may ensue.

Anthony LK, Cindy M, Carol JT, et al. Comparison of nicardipine versus placebo to control hemodynamic responses during emergence and extubation. *J Cardiothorac Vasc Anesth*. 2001;15:704–709.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:558.

Cucchiara RF, Benefiel DJ, Matteo RS, et al. Evaluation of esmolol in controlling increases in heart rate and blood pressure during endotracheal intubation in patients undergoing carotid endarterectomy. *Anesthesiology*. 1986;65:528–531.

Gold MI, Sacks DJ, Grosnoff DB, et al. Use of esmolol during anesthesia to treat tachycardia and hypertension. *Anesth Analg*. 1989;68:101–104.

Helfman SM, Gold MI, Delisser EA, et al. Which drug prevents tachycardia and hypertension associated with tracheal intubation: lidocaine, fentanyl, or esmolol? *Anesth Analg*. 1991;72:482–486.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone; 2008:94–97.

Kapnoudhis P, Vaghadia H, Jenkins LC, et al. Esmolol versus fentanyl for preventing haemodynamic response to intubation in cardiovascular disease. *Can J Anaesth*. 1990;37:S145.

Martin DE, Rosenberg H, Aukburg SJ, et al. Low-dose fentanyl blunts circulatory responses to tracheal intubation. *Anesth Analg*. 1982;61:680.

Sladen RN. Perioperative hypertension. *IARS review course lectures*. Cleveland: International Anesthesia Research Society; 2002:100–114.

Song D, Singh H, White PF, et al. Optimal dose of nicardipine for maintenance of hemodynamic stability after tracheal intubation and skin incision. *Anesth Analg*. 1997;85:1247–1511.

Stoelting RK. Blood pressure and heart rate changes during short-duration laryngoscopy for tracheal intubation: influence of viscous or intravenous lidocaine. *Anesth Analg*. 1978;57:197.

C.7. After induction and intubation, the BP decreased to 70/40 mm Hg. What would you do?

Hypotension after induction of anesthesia is usually due to combination of vasodilation, hypovolemia, and cardiac depression. Vasodilation can be caused by inducing

agents such as thiopental, propofol, diazepam, or midazolam; moderate-to-high doses of narcotics; and potent inhalation agents. Hypertensive patients are in relative hypovolemia because of chronic vasoconstriction and/or diuretic therapy. Preoperative bowel preparation and nothing by mouth further contribute to hypovolemia. Barbiturates, benzodiazepines, and inhalation agents can cause a mild-to-moderate degree of cardiac depression.

Hypotension after induction of anesthesia usually can be easily corrected by volume replacement and simultaneous titration of vasopressors such as ephedrine 5 to 10 mg or phenylephrine in 0.1-mg increments.

Coriat P, Richters C, Douraki T, et al. Influence of chronic angiotensin-converting enzyme inhibition on anesthetic induction. *Anesthesiology*. 1994;81:299–307.

C.8. What is your choice of agents for maintenance of anesthesia? Why?

No particular anesthetic technique or specific drug combinations have been demonstrated to be superior to others in hypertensive patients. Potent inhalation anesthetics or narcotics should be titrated to the desired level of central nervous system depression while the BP is monitored continuously.

Narcotics and nitrous oxide provide an anesthetic with less overall lability of BP, but commonly intraoperative hypertension is difficult to control by moderate doses of narcotics. High doses of narcotics are not suitable for early extubation. Likewise, use of nitrous oxide is debatable in open cholecystectomy given its propensity to increase bowel distention—the severity being related to higher concentration of nitrous oxide and to longer duration of use. This concern is less pertinent for laparoscopic cholecystectomy whereby insufflation of gas to pressurize the abdomen should counteract the distensible property of nitrous oxide (also see Chapter 26, section C.8).

Potent inhalation agents provide greater control of hypertension but seem to produce less stability. Isoflurane, desflurane, and sevoflurane possess the advantage of more peripheral vasodilation and less cardiac depression.

Akca O, Lenhardt R, Fleischmann E, et al. Nitrous oxide increases the incidence of bowel distension in patients undergoing elective colon resection. *Acta Anaesthesiol Scand*. 2004;48(7):894–898.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone; 2008:94–97.

Taylor E, Feinstein R, White PF. Anesthesia for laparoscopic cholecystectomy. Is nitrous oxide contraindicated? *Anesthesiology*. 1992;76(4):541–543.

C.9. How would you manage fluid therapy for hypertensive patients?

Patients with essential hypertension are usually hypovolemic because of vasoconstriction and diuretic therapy. Hydration of the hypertensive patient should be started before induction of anesthesia to minimize the "roller-coaster" often seen with hypertension. However, overhydration should be avoided because it may contribute to postoperative hypertension when the vasodilating effects of anesthetics are gone. Therefore, careful estimation of fluid intake and output is essential. Foley catheter and central venous pressure monitor are indicated for major surgery with extensive fluid exchange.

As discussed previously, presence of LVH in hypertensive patients shifts the left ventricular compliance curve upward and leftward such that for the same ventricular volume, a higher left ventricular diastolic pressure is attained as compared to a nonhypertrophied ventricle. When managing these patients with a PAC, higher pulmonary

artery occlusion pressure (sometimes >20 mm Hg) is necessary to achieve normovolemia. Cardiac output also must be checked frequently during volume challenges.

Fontes ML, Bellows W, Ngo L, et al. McSPI Research Group. Assessment of ventricular function in critically ill patients: limitations of pulmonary artery catheterization. *J Cardiothorac Vasc Anesth.* 1999;13:1–8.

Fontes ML, Hines RH. Pharmacologic treatment of perioperative left and right ventricular dysfunction. In: Kaplan JA, Reich DSN, Konstadt SN, eds. *Cardiac Anesthesia.* 4th ed. Philadelphia: Grune & Stratton; 1999:1155–1191.

Murray MJ. Perioperative hypertension. *ASA annual refresher course lectures.* EMPH-Park Ridge, IL: American Society of Anesthesiologists; 2002:512.

C.10. During the surgery, BP increased to 220/120 mm Hg. How would you treat the hypertension?

Intraoperative control of hypertension is outlined in Table 10.4. Severe hypertension that occurs during a surgical procedure is most frequently due to inadequate anesthesia. Inadequate blockade of sensory input from the surgical procedure stimulates the elaboration of sympathomimetic amines, resulting in hypertension and tachycardia. If a potent inhalation anesthetic is being used, the level of anesthesia should be deepened by increasing the inspired concentration of the anesthetic. A narcotic may not control the rise in BP, and it may be necessary to switch to a potent inhalation anesthetic.

Hydralazine, 5-mg increments, may be titrated to decrease BP safely with little chance of excessive reduction. The onset of action is in 10 to 15 minutes with 1 to 2 hours duration.

Labetalol, 5- to 10-mg increments, is very useful in controlling hypertension and tachycardia. It makes the most sense to use β-blockers after a significant rise in BP

Table 10.4 Intraoperative Control of Hypertension

Anesthetics
Narcotics, inhalation agents, butorphanol, lidocaine
Antihypertensives
Adrenergic blockers
α-Blocker: phentolamine
β-Blocker: propranolol, metoprolol
α- and β-blocker: labetalol
Calcium channel blockers
Diltiazem, nicardipine, verapamil
ACE inhibitors
Enalapril
Direct vasodilators
Hydralazine, nitroglycerin, nitroprusside
Dopaminergic agonists
Fenoldopam

ACE, angiotensin-converting enzyme.

because these agents act directly to antagonize the effects of the catecholamines. Although other agents may lower the BP, it is highly possible that the excessive availability of both norepinephrine and epinephrine will continue to exert their effects at the receptor site—compromising tissue perfusion from microcirculatory vasoconstriction. This view may explain the broad anti-ischemic effects of perioperative β-blockers on the brain, the heart, and the kidneys.

Rarely, continuous infusion of nicardipine, nitroglycerin, or nitroprusside, direct arteriolar vasodilators, is needed to control hypertension during anesthesia.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone; 2008:94–97.

Lindenauer PK, Pekow P, Wang K. Perioperative beta-blocker therapy and mortality after major noncardiac surgery. *N Eng J Med*. 2005;353(4):349–361.

Maggio PM, Taheri PA. Perioperative issues: myocardial ischemia and protection-beta-blockade. *Surg Oncol Clin N Am*. 2005;85(6):1091–1102.

Passamonti E, Pirelli S. Reducing risk of cardiovascular events in noncardiac surgery. *Expert Opin Pharmacother*. 2005;6(9):1507–1515.

Sladen RN. Perioperative hypertension. *IARS review course lectures*. Cleveland, OH: International Anesthesia Research Society; 2002:100–114.

C.11. What could you do to prevent hypertension during extubation and emergence?

It is logical to use to use antihypertensive agents during extubation and emergence, as the patient is awakened at the end of surgery. Many drugs or combinations are effective, including intravenous lidocaine, esmolol, labetalol, verapamil, or diltiazem 2 minutes before extubation. If BP goes over desired levels after extubation, additional doses may be titrated to control BP.

Mikawa K, Nishina K, Maekawa N, et al. Attenuation of cardiovascular responses to tracheal extubation: verapamil versus diltiazem. *Anesth Analg*. 1996;82:1205–1210.

Nishina K, Mikawa K, Maekawa N, et al. Attenuation of cardiovascular responses to tracheal extubation with diltiazem. *Anesth Analg*.1995;80:1217–1222.

C.12. Would you consider regional anesthesia for this patient?

Certainly, regional anesthesia can avoid marked increases in sympathetic tone and hemodynamic changes that occur with intubation and extubation. Spinal or epidural anesthesia may be used for lower abdominal surgery. For cholecystectomy, higher levels of regional anesthesia are needed and may compromise respiratory function. Meanwhile, prolonged surgery can cause anxiety and irritability that may induce hypertension and tachycardia.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone; 2008:94–97.

D. Postoperative Management

D.1. The patient developed hypertension, BP 210/110 mm Hg in the post-anesthesia care unit. What would you do?

The management of postoperative hypertension depends on the etiology of the hypertension, the clinical scenario, and the level of hypertension. First, the cause

of hypertension should be determined and treated accordingly. Hypertension per se should also be treated by an antihypertensive agent. The causes of postoperative hypertension include pain, emergence excitement, hypoxemia, hypercarbia, reaction to endotracheal tube, full bladder, hypothermia, relative hypervolemia from intraoperative administration of excess fluid, and chronic medication and withdrawal. The most common cause of postoperative hypertension is incisional pain. As the patient awakens, pain triggers an outpouring of catecholamines. The extreme lability of BP in many hypertensive patients makes this rapid increase critical to control. Depending on the cause of hypertension, intravenous analgesics, and antihypertensives or diuretics should be titrated to control hypertension. If both tachycardia and hypertension occurred postoperatively, calcium channel blockers such as verapamil, diltiazem, or nicardipine and β-blocking agents such as propranolol, esmolol, labetalol, or metoprolol are preferred agents. Hypertension resulting from pain can be preventable or attenuated by asking the surgeon to inject a long-lasting local anesthetic along the incision or to perform a local nerve block.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1117.

CHAPTER 11

Cardiac Tamponade

MANUEL L. FONTES, NIKOLAOS SKUBAS, AND JAMES OSORIO

A 69-YEAR-OLD WOMAN

was presented with shortness of breath, inability to lie supine, oliguria, and overt weakness, 4 days after two-vessel coronary artery bypass graft procedure and replacement of a mitral valve. On examination, she appeared anxious and diaphoretic with the following vital signs: respiratory rate, 38 breaths per minute; heart rate (HR), 120 beats per minute (normal sinus rhythm); and systemic blood pressure, 115/66 mm Hg. A pulmonary artery catheter (PAC) was placed and revealed: pulmonary artery (PA) pressures, 55/15 mm Hg; pulmonary artery occlusion pressure (PAOP), 14 mm Hg; central venous pressure (CVP), 23 mm Hg; and cardiac output (CO), 2.7 L per minute. Both the prothrombin and the partial thromboplastin times (PTTs) were elevated.

A. Medical Disease and Differential Diagnosis

1. What is the differential diagnosis of low CO postoperatively?
2. What is cardiac tamponade? Enumerate the common etiologies.
3. What is the difference between acute and delayed cardiac tamponade?
4. How is postcardiotomy cardiac tamponade diagnosed?
5. What is regional cardiac tamponade?
6. What is pulsus paradoxus? What is Kussmaul sign?
7. Describe ventricular interaction in cardiac tamponade.
8. How is coronary blood flow affected in cardiac tamponade?
9. What are the electrocardiographic abnormalities associated with cardiac tamponade?
10. What radiographic and echocardiogram findings are noted in cardiac tamponade?
11. What is in the differential diagnosis of postcardiopulmonary bypass (post-CPB) bleeding?

12. What is the mechanism of action of low molecular weight heparin (LMWH)?
13. Describe the advantages of LMWH therapy over standard heparin therapy.
14. What is heparin-induced thrombocytopenia (HIT)? How is the diagnosis made?
15. What is the therapy for HIT?
16. Can HIT be caused by LMWH?
17. What is the mechanism of heparin antagonism by protamine?
18. What is "heparin rebound"?
19. How does warfarin affect the coagulation system? What is the therapy for reversing its effect?
20. What do the following measure: prothrombin time (PT), activated partial thromboplastin time (aPTT), thrombin time, activated clotting time (ACT)?
21. How is the anticoagulant effect of LMWH monitored?
22. What is point-of-care testing (POCT) and what are the commonly used point-of-care devices?
23. How does desmopressin aid hemostasis?
24. What is fibrinolysis?
25. What is aminocaproic acid? What is tranexamic acid?

B. Preoperative Evaluation and Preparation

1. Interpret the hemodynamic findings of this patient.
2. How would you treat the low output status of this patient?
3. How would you evaluate this patient's coagulation status?
4. What do fresh frozen plasma (FFP) and cryoprecipitate contain?
5. What are the indications for transfusing FFP, platelet concentrate, and cryoprecipitate?
6. What are the complications associated with blood component transfusions?
7. What is the risk of acquiring human HIV from blood exposure?
8. Assuming that the patient has cardiac tamponade, how would you prepare this patient for surgery?

C. Intraoperative Management

1. How would you monitor this patient during transport to the operating room? What emergency drugs would you bring with you?
2. In this patient, what hemodynamic effects would occur from intravenous induction with ketamine, thiopental, fentanyl, propofol, etomidate, or midazolam?
3. Describe the induction process for cardiac tamponade.
4. Following induction and intubation, the systemic blood pressure decreased to 55/30 mm Hg. Describe the clinical events accounting for this perturbation and the management steps required for resuscitation.
5. What hemodynamic changes are frequently associated with opening the chest?
6. What is myocardial stunning? What is myocardial hibernation?

D. Postoperative Management

1. How would you manage hypertension in the intensive care unit (ICU)?
2. When would it be appropriate to extubate this patient?

A. Medical Disease and Differential Diagnosis

A.1. What is the differential diagnosis of low CO postoperatively?

CO is the product of stroke volume (SV) and HR (CO = HR × SV). Therefore, a low output state can occur when SV and/or HR decrease. Fast HRs, of either ventricular or atrial origin (i.e., atrial fibrillation) can also cause a low output state because the diastolic filling time is decreased or the atrial contribution to the ventricular filling is reduced or abolished. Because SV is the difference between left ventricular end-diastolic volume and left ventricular end-systolic volume, the etiology of a reduced SV can be more accurately determined by exploring whether there has been a change in the preload (left ventricular end-diastolic volume), the afterload, and/or the contractile state of the left ventricle. Either too much preload (that may cause ventricular over-distention and systolic dysfunction) or too little preload can lower the CO. Myocardial contractility can be compromised by either direct causes (myocardial ischemia, myocardial infarction, myocardial stunning, or myocardial hibernation) or indirect causes (mechanical factors as in cardiac tamponade, pulmonary embolism; pharmacologic agents; and by toxins, namely, inflammatory cytokines and bacterial endotoxins). A combination of different hemodynamic disturbances can coexist in the same patient. For example, a patient can have both a decrease in contractility and a reduced preload to account for the low output state. Therefore, correcting one problem alone may not produce the optimal hemodynamic condition.

Ghobashy A, Fontes M, Hines R. Cardiogenic shock. In: Murray MJ, Coursin DB, Pearl RG, et al., eds. *Critical Care Medicine: Perioperative Management*. 2nd ed. Philadelphia: Lippincott Williams & Wilkins; 2002.

Pagel PS. Cardiac physiology. In: Kaplan JA, Reich DL, Savino JS, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: WB Saunders; 2011:98–131.

A.2. What is cardiac tamponade? Enumerate the common etiologies.

Cardiac tamponade is defined as significant extrinsic compression of the heart by accumulating intrapericardial blood and clots (postcardiotomy, chamber perforation, dissecting aortic aneurysm, trauma, anticoagulant therapy), exudative effusions (malignant states, infective pericarditis, idiopathic pericarditis), nonexudative effusions (uremia, systemic lupus erythematosus, rheumatoid arthritis, idiopathic, radiation), and air. Irrespective of the actual volume, if the intrapericardial pressure is increased enough, globally or regionally, the risk for cardiac tamponade exists. The level of significance of cardiac tamponade depends on whether the definition is clinical or physiologic. Cardiac tamponade is a pathophysiologic continuum that on one extreme may be clinically insignificant and on the other extreme presents as a life-threatening condition requiring emergent surgical attention. Clinical tamponade is frequently associated with marked increase in pericardial pressure relative to atrial and ventricular intracardiac pressures such that SV progressively declines, resulting in systemic hypotension and cardiogenic shock.

Fowler NO, Gabel M, Buncher CR. Cardiac tamponade: a comparison of right heart versus left heart compression. *J Am Coll Cardiol*. 1988;12:187–193.

Oliver WC Jr, Nuttall GA. Uncommon cardiac diseases. In: Kaplan JA, Reich DL, Savino JS, et al., eds. *Kaplan's Cardiac Anesthesia*. 5th ed. Philadelphia: WB Saunders; 2011:710–713.

Spodick DH. Pathophysiology of cardiac tamponade. *Chest*. 1998;113:1372–1378.

Skubas NI, Fontes ML. Pericardial diseases. In: Mathew J, Swaminathan M, Ayoub C, eds. *Clinical Manual and Review of Transesophageal Echocardiography*. New York: McGraw-Hill; 2010:351–369.

A.3. What is the difference between acute and delayed cardiac tamponade?

In the setting of cardiac surgery, acute cardiac tamponade can occur over minutes, hours, or after a few days postoperatively. The reported incidence of acute cardiac tamponade is 0.5% to 5.8%. In the typical patient, a significant chest tube output (greater than 200 mL per hour) in the immediate postoperative period, with or without hemodynamic signs of inadequate CO, is a sign of an increased amount of blood around the heart. Alternatively, the chest tubes may become clogged by blood clots impeding mediastinal drainage and the clinical picture of cardiac tamponade develops sooner. Delayed tamponade has been arbitrarily defined as cardiac tamponade occurring 5 to 7 days after pericardiotomy. The incidence is 0.3% to 2.6%. It is often misdiagnosed because of a low index of suspicion and because the clinical signs and symptoms can be comparable to those of congestive heart failure, pulmonary embolism, and generalized fatigue (i.e., failure to thrive postoperatively). The most common culprit in delayed cardiac tamponade is anticoagulant therapy with warfarin (Coumadin), heparin, or platelet-inhibiting agents. However, a pericardial effusion (PE) after cardiac surgery is common. Using echocardiography, Weitzman et al. evaluated 122 consecutive patients postoperatively and demonstrated that most of them (103/122, 84%) had PEs. Generally, effusions reach their maximum size by the 10th postoperative day and regress spontaneously thereafter.

D'Cruz IA, Overton DH, Pai GH. Pericardial complications of cardiac surgery: emphasis on the diagnostic role of echocardiography. *J Card Surg*. 1992;7:257–268.

Nelson RM, Jenson CB, Smoot WM III. Pericardial tamponade following open-heart surgery. *J Thorac Cardiovasc Surg*. 1969;58:510–516.

Weitzman LB, Tinker WP, Kronzon I, et al. The incidence and natural history of pericardial effusions after cardiac surgery: an echocardiographic study. *Circulation*. 1984;69:506–511.

A.4. How is postcardiotomy cardiac tamponade diagnosed?

The diagnosis of cardiac tamponade following cardiac surgery is often difficult to make and requires a high degree of clinical suspicion, physical examination, proficient knowledge of PAC-derived measurements, and diagnostic tools such as echocardiography and chest radiography. Often, the diagnosis is made in the operating room, whereby evacuation of clot and blood from the mediastinum is associated with a drastic improvement in hemodynamics (Fig. 11.1). Relying on one modality alone for diagnosis can lead to inaccurate management decisions and increase patient morbidity. For example, the PAC is an important device for monitoring cardiac function; however, its measures can be misleading postcardiotomy unless the clinician is aware of its limitations. The classical teaching of equalization of diastolic blood pressures in cardiac tamponade (CVP = pulmonary artery diastolic pressure [PAD] = PAOP) is infrequently observed postoperatively because the previously transected pericardium is left open. Thus, blood or clot or both do not distribute homogeneously around the heart to produce equalization of pericardial diastolic pressures. Generally, the CVP is elevated but the PAD and the PAOP can be normal, elevated, or, in some cases, reduced. With significant compression of the right heart, reduced blood flow to the PA and to the left heart can yield low left-sided heart pressures that would be inconsistent with "classical" tamponade physiology. Russo et al. found that only 33% of patients with the diagnosis of postoperative cardiac tamponade had right heart catheterization findings that reflected equalization of diastolic blood pressures. Overall, 90% of patients with postcardiotomy cardiac tamponade had atypical clinical, hemodynamic, and/or echocardiographic findings. Therefore,

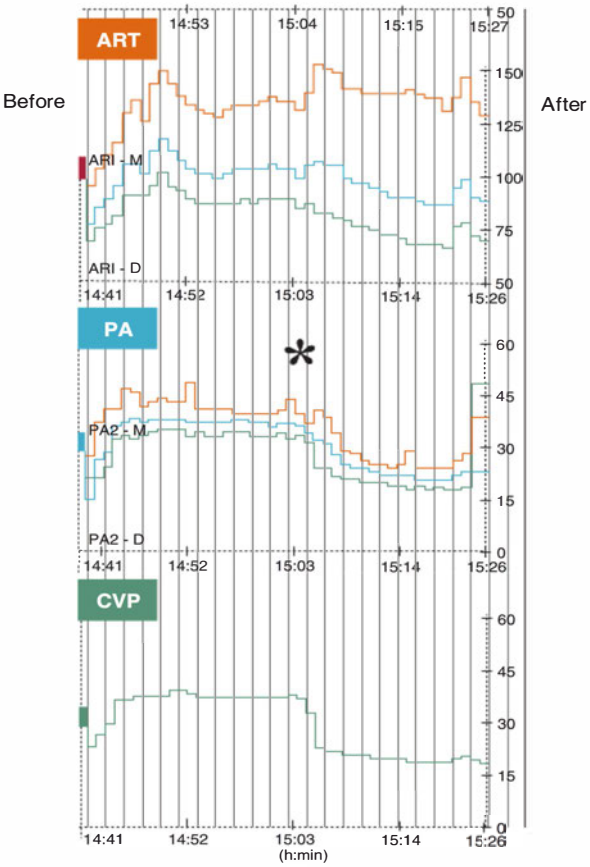


Figure 11.1 Intraoperative hemodynamics before and after evacuation of pericardial fluid. Arterial blood pressure (ART), pulmonary artery pressure (PA), and central venous pressure (CVP) are shown during chest exploration for cardiac tamponade. Note the elevated diastolic PA and CVP at the beginning of the anesthetic (left hand of the pressure trends). There is equalization of CVP and diastolic PA pressure, suggesting global pericardial effusion. As soon as the chest was opened and the pericardial collection was evacuated (*asterisk*), the ART increased abruptly and the pulse pressure widened, although both PA and CVP immediately decreased to normal levels. Taking into consideration that ART increased whereas CVP decreased after evacuation of the pericardial collection; one can assume that the cardiac output has increased.

the diagnosis of postoperative cardiac tamponade should be considered every time hemodynamic deterioration is encountered, particularly when reduction in CO or blood pressure or both are not readily responsive to conventional management. Furthermore, in delayed tamponade, the complaints tend to be vague and invasive hemodynamic data (i.e., PAC) is usually not available to allow prompt diagnosis of tamponade. Whenever the patient is not progressing as expected postoperatively and signs of end-organ dysfunction (fall in urine output or increase blood urea nitrogen and creatinine) are present, an echocardiogram should be obtained to rule out cardiac tamponade.

Russo AM, O'Connor WH, Waxman HL. Atypical presentations and echocardiographic findings in patients with cardiac tamponade occurring early and late after cardiac surgery. *Chest*. 1993;104:71–78.

Spodick D. Pathophysiology of cardiac tamponade. *Chest*. 1998;113:1372–1378.

A.5. What is regional cardiac tamponade?

Regional cardiac tamponade occurs when one or more cardiac chambers (and not necessary the entire heart) become compressed by blood or blood clot or both, thereby compromising heart function (Figs. 11.2 and 11.3). Postcardiotomy, the diastolic regional collapse of the right atrium or the right ventricle is the most common echocardiographic finding in "early" cardiac tamponade. Postoperatively, a right atrial hematoma often becomes localized around the anterior and lateral walls. Clots can also be found behind the left atrium where they become encysted in the oblique sinus. Selective compression of the right heart by hematoma becomes less prominent in "delayed" tamponade, as the right heart becomes adherent or tethered to the anterior chest wall. As discussed in the previous answer, the diagnosis of tamponade is often misdiagnosed because the classical features of tamponade are often absent and blood and blood clots are unevenly distributed around the heart. The clinical presentation may be mistaken for congestive heart failure, acute left or right ventricular dysfunction, septic shock, or pulmonary embolism.

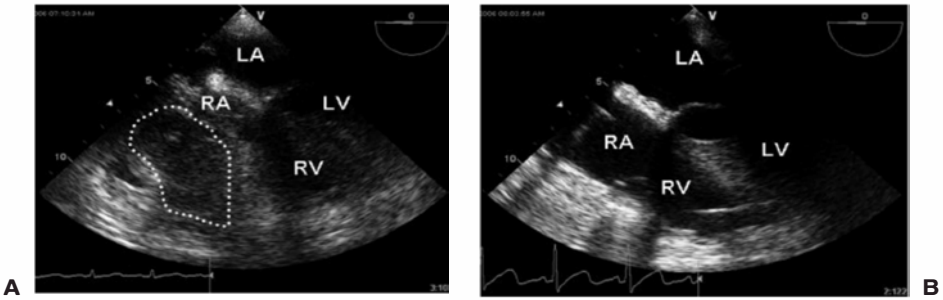
Chuttani K, Pandian NG, Mohanty PK, et al. Left ventricular diastolic collapse: an echocardiographic sign of regional cardiac tamponade. *Circulation*. 1991;83:1999–2006.

Jadhav P, Asirvatham S, Craven P, et al. Unusual presentation of late regional cardiac tamponade after aortic surgery. *Am J Card Imaging*. 1996;10:204–206.

Kochar GS, Jocab LE, Holter MN. Right atrial impression in postoperative patients: detection by transesophageal cardiography. *J Am Coll Cardiol*. 1990;16:511–516.

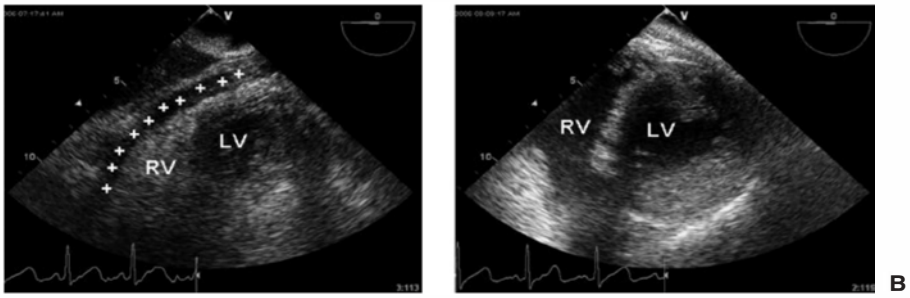
Russo AM, O'Connor WH, Waxman HL. Atypical presentations and echocardiographic findings in patients with cardiac tamponade occurring early and late after cardiac surgery. *Chest*. 1993;104:71–78.

Sandifer DP, Gonzalez JL. Refractory postoperative hypoxemia associated with regional cardiac tamponade and patent foramen ovale. *Crit Care Med*. 1997;25:1608–1611.



A B

Figure 11.2 Regional, acute pericardial effusion. The heart is viewed in the mid-esophageal four-chamber view at 0-degree rotation, before **(A)** and after **(B)** evacuation of a loculated pericardial clot. The pericardial collection (*dotted line*) is around the right atrium (RA), almost obliterating its cavity (compared with the size of RA after evacuation). The collection is partially compressing the cavity of the right ventricle (RV). LA, left atrium; LV, left ventricle.



A B

Figure 11.3 Pericardial effusion. The heart is viewed in the transgastric mid-papillary, short-axis view, before **(A)** and after **(B)** the evacuation of a posterior pericardial collection (*asterisks*). Notice the increase in cavity size of the left ventricle (LV) and reappearance of the cavity of the right ventricle (RV) after evacuation of the pericardial collection.

Skubas NI, Fontes ML. Pericardial diseases. In: Mathew J, Swaminathan M, Ayoub C, eds. *Clinical Manual and Review of Transesophageal Echocardiography*. 2nd ed. New York: McGraw-Hill; 2010:351–369.

A.6. What is pulsus paradoxus? What is Kussmaul sign?

Normally, during spontaneous inspiration, the extrathoracic to intrathoracic pressure gradient is increased and the filling of the right heart is slightly larger than the filling of the left heart. In the latter, the decreased intrapulmonary pressure during inspiration will cause a relative "pooling" of the blood in the lungs and decreases the filling gradient. That causes an inspiratory fall of less than 10 mm Hg in the arterial systolic pressure along with an accompanying inspiratory fall in the venous pressure. A paradoxical pulse differs from the normal situation in two aspects: the inspiratory fall of the arterial pressure exceeds 10 mm Hg and the inspiratory venous pressure remains steady or increases (Kussmaul sign), instead of decreasing. Echocardiographic studies of patients with cardiac tamponade by D'Cruz et al. described phasic respiratory changes whereby both left ventricular dimensions and mitral valve excursion decreased during inspiration. In contrast, right ventricular dimensions increased in association with a shifting of the interventricular septum toward the left ventricle. That is, the right heart filling is done at the expense of the left. Of importance, pulsus paradoxus is not unique to cardiac tamponade. The phasic respiratory changes in ventricular dimensions with exaggerated decrease in systemic systolic arterial pressure during inspiration can be present in a variety of clinical conditions such as respiratory distress, airway obstruction, chronic obstructive pulmonary disease, and pulmonary embolism. A prominent feature of cardiac tamponade, pulsus paradoxus, may not be present at all in patients with chest wall trauma, neuromuscular disease, and pneumothorax because these patients cannot generate sufficient negative intrapleural pressure during inspiration to produce the typical changes in chamber dimension and the fall in left ventricular SV. Similarly, those who are receiving positive pressure mechanical ventilation (early postoperative period) and patients with severe aortic regurgitation do not exhibit pulsus paradoxus.

D'Cruz IA, Overton DH, Pai GM. Pericardial complications of cardiac surgery: emphasis on the diagnostic role of echocardiography. *J Card Surg.* 1992;7:257–268.

Frey B, Freezer N. Diagnostic value and pathophysiologic basis of pulsus paradoxus in infants and children with respiratory disease. *Pediatr Pulmonol.* 2001;31:138–143.

Skubas NI, Fontes ML. Pericardial diseases. In: Mathew J, Swaminathan M, Ayoub C, eds. *Clinical Manual and Review of Transesophageal Echocardiography*. New York: McGraw-Hill; 2010:351–369.

A.7. Describe the ventricular interaction in cardiac tamponade.

Ventricular interaction is extremely important for the maintenance of adequate cardiac performance. Under normal conditions, the average SV of the right ventricle equals the SV of the left ventricle; however, cyclical respiratory differences in left and right ventricular SV do occur. During inspiration, the generated negative intrapleural pressure facilitates blood return to the right heart, whereas blood return to the left heart is diminished for the following reasons: (1) lung expansion increases its reservoir for blood and (2) the increase in right ventricular filling causes the interventricular septum to "bulge" leftward, thereby reducing left ventricular dimensions and altering its compliance and filling (ventricular interaction). During exhalation, the reverse process occurs. In the case of cardiac tamponade, the ventricular interaction is augmented and involves not only the interventricular septum but also other chambers depending on the etiology of the tamponade (fluid versus clot, regional versus global tamponade). Fundamentally, as intrapericardial content increases, it will reach a point whereby the parietal pericardium cannot stretch to accommodate the rising pressure. Because of the fixed space within the pericardium, the cardiac chamber dimensions become smaller as the pericardial contents increase. First, the thin-walled and more compliant atria progressively gets compressed, followed by the right ventricle, and finally by the left ventricle. Overall, the physiology of ventricular interaction in clinical cardiac tamponade becomes complex as the pressure–volume relation of mediastinal and chest structure alters with each heartbeat and from respiratory and neuroendocrine influences.

Spodick DH. Pathophysiology of cardiac tamponade. *Chest*. 1998;113:1372–1378.

A.8. How is coronary blood flow affected in cardiac tamponade?

In the absence of coronary artery disease, coronary blood flow is reduced in cardiac tamponade, but this reduction is not sufficient to add an ischemic insult to the heart, because there is a proportionate decrease in ventricular preload (underfilled heart) and ventricular afterload. Consequently, both myocardial work and oxygen consumption are reduced. In contrast, patients with coronary artery disease may be at increased risk for myocardial ischemia and infarction.

Reddy PS, Curtiss EL, O'toole JD, et al. Cardiac tamponade: hemodynamic observations in man. *Circulation*. 1978;58:265–272.

A.9. What are the electrocardiographic abnormalities associated with cardiac tamponade?

Electrocardiographic changes may occur in the setting of cardiac tamponade. These include nonspecific ST-T wave abnormalities, low-voltage QRS complex, signs of myocardial ischemia and pericarditis, and electrical alternans (Fig. 11.4). The latter is seen in patients with large effusions and is characterized by beat-to-beat shifts in electrical axis. This beat-to-beat alteration may be due to increased distance between the heart and the chest wall resulting in a "pendulum" like motion of the heart. However, it has been shown that with minimal amount of pericardial fluid removal, the presence of electrical alternans can be abolished while the pericardial space remains enlarged. Therefore, the electrocardiographic change of electrical alternans may reflect a

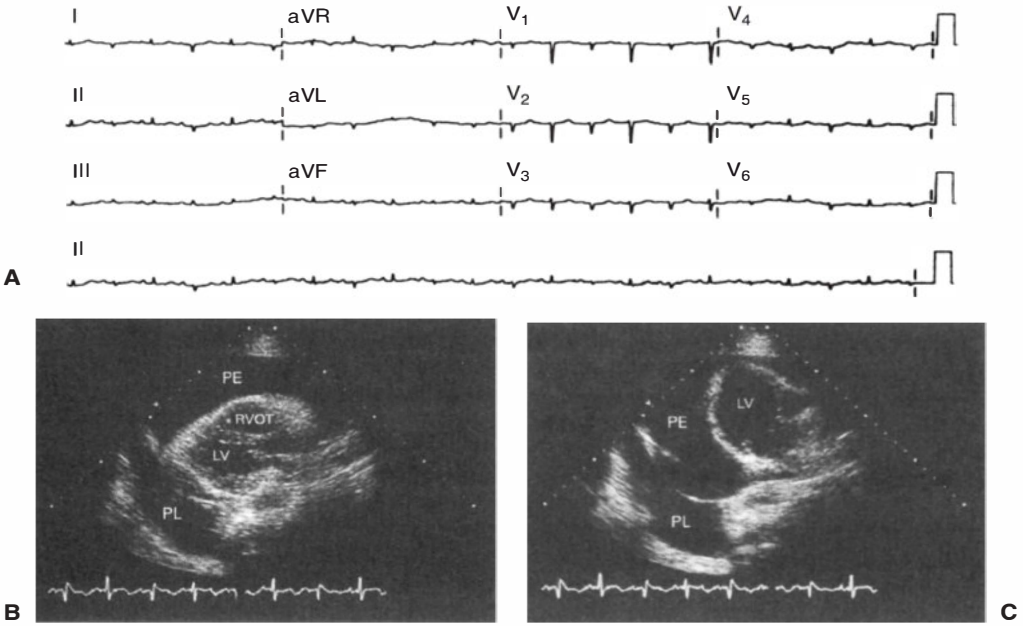


Figure 11.4 Depiction of electrical alternans in a patient with cardiac tamponade **(A)**. The images demonstrate significant pericardial effusions (PE) obtained during transthoracic echocardiography. Note the image of the left ventricle (LV) during systole **(B)** and diastole **(C)**. PL, pleural effusion; RVOT, right ventricular outflow tract. (From Longo MJ, Jaffe CC. Images in clinical medicine: electrical alternans. *N Engl J Med*. 1999;341:2060, with permission)

hemodynamic pathology rather than an anatomic abnormality. This finding, although sensitive for cardiac tamponade, is not very specific (very few patients with tamponade present with electrical alternans).

Fox JJ, McHarg JL, Gilmour RF Jr. Ionic mechanism of electrical alternans. *Am J Physiol Heart Circ Physiol*. 2002;282:H516-H530.

Kosta E, Kronzon I. Electrical alternans in cardiac tamponade. *Echocardiography*. 2000;17(6 Pt 1):575–576.

Longo MJ, Jaffe CC. Images in clinical medicine: electrical alternans. *N Engl J Med*. 1999;341:2060.

A.10. What radiographic and echocardiographic findings are noted in cardiac tamponade?

On standard anterior-posterior chest radiography, the cardiac silhouette may appear normal in size or extremely enlarged, depending on the acuity and chronicity of the tamponade process. Normally, the pericardial fluid amounts to 15 to 25 mL. Acute tamponade physiology can arise with as little as 150 mL of effusion, whereas chronic effusions may exceed 1,000 mL before clinical signs and symptoms of cardiac tamponade become evident. In the latter case, on chest radiography film, the cardiac silhouette will appear "widened" with or without features such as obscuring of the pulmonary vessels at the hilum and a globular or "water bottle" configuration of the heart.

Transthoracic or transesophageal echocardiography can differentiate between cardiac dysfunction arising from direct myocardial injury and cardiac dysfunction associated with mechanical processes. Pericardial effusions can be readily seen and semi quantitated. Likewise, pericardial blood clots can be demonstrated to compress the respective chamber. Additional echocardiographic signs observed in tamponade include (1) diminished left ventricular dimension and mitral valve excursion during inspiration, (2) shifting of the interventricular septum toward the left ventricle, (3) transvalvular (mitral and aortic) flow characteristics seen by Doppler techniques, (4) diastolic posterior motion of the right ventricular wall, and (5) in some cases, a systolic notch on the right ventricular epicardium (Figs. 11.2 and 11.3). Although many of the findings of both radiographic film and echocardiogram can be suggestive of cardiac tamponade, not a single sign is 100% sensitive and specific.

Oliver WC Jr, Nutall GA. Uncommon cardiac diseases. In: Kaplan JA, Reich DL, Savino JS, et al., eds. *Kaplan's Cardiac Anesthesia*. 5th ed. Philadelphia: WB Saunders; 2011:710–713.

Singh S, Wann LS, Schuchard GH, et al. Right ventricular and right atrial collapse in patients with cardiac tamponade—a combined echocardiographic and hemodynamic study. *Circulation*. 1984;70:996–971.

Skubas NI, Fontes ML. Pericardial diseases. In: Mathew J, Swaminathan M, Ayoub C, eds. *Clinical Manual and Review of Transesophageal Echocardiography*. 2nd ed. New York: McGraw-Hill; 2010:351–369.

A.11. What is in the differential diagnosis of postcardiopulmonary bypass (post-CPB) bleeding?

Significant bleeding following cardiac surgery requiring surgical exploration "bring-back" occurs in approximately 3% of cases. Often, the source of bleeding cannot be ascertained and its etiology is ascribed to a coagulation defect. Procedures that require cardiopulmonary bypass (CPB) are known to adversely affect the hemostatic mechanisms, including vascular endothelium, fibrinolytic and coagulation factors, platelet, plasminogen, and inflammatory pathways (Fig. 11.5). Under normal settings, these systems (and others yet unknown) act in concert and in opposition with one another to prevent bleeding by promoting clot formation at the site of endothelial injury (procoagulant effects) and prevent or destroy clot formation (anticoagulant effects—either directly or indirectly through inhibitory mediators). Once blood elements come in contact with a nonendothelialized surface (bypass circuit), the procoagulant system becomes activated, resulting in consumption of platelets, coagulation factors, and fibrinogen (tissue factor pathway). The potential for postoperative bleeding will depend on the degree of activation and pre-existing levels of the procoagulants as well as other factors such as the duration of CPB, systemic hypothermia, comorbid states (renal and liver insufficiency), type of surgery (reoperation, circulatory arrest, combined procedures), and prior or current treatment with anticoagulant (platelet inhibitors, warfarin process). Once activated, they secrete several types of granules. Granules, containing peptides such as fibrinogen, thrombospondin, factors V and VIII, and β-thromboglobulin, are reduced in both number and content during CPB. Of greater importance is the loss of several membrane glycoproteins (IIb-IIIa) that interact with fibrinogen and other cellular elements, allowing for platelet conjugation and propagation of clot formation. Overall, postcardiotomy bleeding is due to (1) a qualitative and a quantitative platelet defect, (2) deficiency, and (3) surgical bleeding. The latter can arise from either venous or arterial sources that were undetected before closure of the chest. Attentive and meticulous effort to surgical hemostasis can significantly reduce the incidence of bring backs.

Despotis GJ, Avidan MS, Hogue CW Jr. Mechanisms and attenuation of hemostatic activation during extracorporeal circulation. *Ann Thorac Surg*. 2001;72:S1821–S1831.

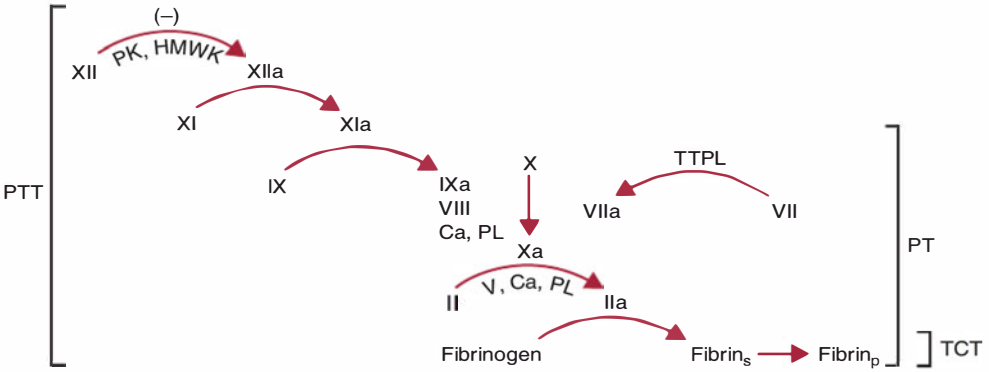


Figure 11.5 The coagulation cascade, illustrating the coagulation factors required for various screening tests. HMWK, high molecular weight kininogen; PK, prekallikrein; PL, phospholipid by platelets; PT, prothrombin time; PTT, partial thromboplastin time; TCT, thrombin clotting time; TTPL, tissue thromboplastin; fibrins, fibrin single standards; fibrinp, fibrin polymer. (From Coleman RW, Hirsch J, Marder VJ, et al., eds. *Hemostasis and Thrombosis: Basic Principles and Clinical Practice*. 2nd ed. Philadelphia: JB Lippincott; 1987:1052, with permission)

Levy JH. Pharmacologic preservation of the hemostatic system during cardiac surgery. *Ann Thorac Surg*. 2001;72:S1814–S1820.

Spiess BD, Horrow J, Kaplan JA. Transfusion medicine and coagulation disorders. In: Kaplan JA, Reich DL, Savino JS, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: WB Saunders; 2011:949–984.

A.12. What is the mechanism of action of low molecular weight heparin (LMWH)?

Unfractionated heparin exerts its anticoagulant activity through antithrombin III (ATIII). ATIII inhibits thrombin (factor IIa) and factors IXa, Xa, and XIa. Unfractionated heparin accelerates the formation of ATIII-IIa complex by 2,000 folds (and that requires the simultaneous binding of unfractionated heparin of at least 18 saccharide units–length to both ATIII and IIa), and the formation of ATIII-Xa by 1,200 folds. LMWHs are fragments of unfractionated heparin produced by controlled enzymatic or chemical depolymerization processes yielding chains having molecular weight of 6,000 to 7,000 daltons. LMWHs consist of 8 to 16 saccharide units and inhibits factor Xa preferentially. This inhibition requires only that LMWH binds to ATIII and the latter interacts with factor Xa, without the interaction between LMWH and factor Xa being necessary. LMWH has greater inhibitory effect on factor Xa, whereas unfractionated heparin exerts an equipotent effect against both thrombin and factor Xa. The aPTT monitors the anti-IIa activity more closely than the anti-Xa activity. Finally, both LMWH and unfractionated heparin cause release of tissue factor pathway inhibitor from vascular endothelium, which then forms a complex with and inhibits factor Xa. This complex in turn inactivates factor VIIa.

Clark SC, Vitale N, Zacharias J, et al. Effect of low molecular weight heparin (fragmin) on bleeding after cardiac surgery. *Ann Thorac Surg*. 2000;69:762–765.

Gohlke-Bärwolf C. Anticoagulation in valvar heart disease: new aspects and management during non-cardiac surgery. *Heart*. 2000;84:567–572.

Harenberg J. Pharmacology of low molecular weight heparins. *Semin Thromb Hemost.* 1990;16:12–18.

Spiess BD, Horrow J, Kaplan JA. Transfusion medicine and coagulation disorders. In: Kaplan JA, Reich DL, Savino JS, et al., eds. *Kaplan's Cardiac Anesthesia.* 6th ed. Philadelphia: WB Saunders; 2011:949–984.

Weitz JI. Drug therapy: low molecular weight heparins. *N Engl J Med.* 1997;337:688–698.

A.13. Describe the advantages of LMWH over standard heparin therapy.

There are several clinical and pharmacologic advantages of LMWH over unfractionated heparin. The plasma half-life of LMWH is two to four times longer than unfractionated heparin, which undergoes a dose-dependent elimination by the liver and the kidneys. A significant amount of unfractionated heparin is bound to plasma proteins, vascular endothelium, and macrophages, resulting in less bioavailability and an unpredictable anticoagulant effect. Consequently, careful laboratory monitoring is required. Additional benefits of LMWH over unfractionated heparin include less bleeding (less platelet inhibition and decreased propensity for increased microvascular permeability). Several clinical trials have improved the efficacy and safety of LMWH over unfractionated heparin. Of note, LMWH is not recommended in the setting of renal failure. The anticoagulant activity of LMWH may be measured by assaying factor Xa levels. Many different types of LMWH are available, each having slightly different pharmacologic effects (bioavailability, anticoagulant effect). Our understanding of the anticoagulant mechanism of LMWH continues to evolve and, although its indications continue to broaden, there may be safety concerns that ought not to be dismissed.

Alban S, Gastpar R. Plasma levels of total and free tissue factor pathway inhibitor (TFPI) as individual pharmacological parameters of various heparins. *Thromb Haemost.* 2001;85:824–829.

Cohen AT, Bailey CS, Alikhan R, et al. Extended thromboprophylaxis with low molecular weight heparin reduces symptomatic venous thromboembolism following lower limb arthroplasty: a meta-analysis. *Thromb Haemost.* 2001;85:940–941.

Huse DM, Cummins G, Taylor DC, et al. Outpatient treatment of venous thromboembolism with low-molecular-weight heparin: an economic evaluation. *Am J Manage Care.* 2002;8(suppl 1):S10–S16.

Kleinschmidt K, Charles R. Pharmacology of low molecular weight heparins [review]. *Emerg Med Clin North Am.* 2001;19:1025–1049.

A.14. What is heparin-induced thrombocytopenia (HIT)? How is the diagnosis made?

Heparin normally binds to platelet membranes at GPIb and other receptor sites and aggregates normal platelets by releasing adenosine diphosphate. HIT is a serious complication of heparin therapy that is predominantly immune-mediated by a binary complex formed between heparin and platelet factor 4. The reaction is commonly caused by an immunoglobulinG antibody that binds and activates platelets in the presence of heparin. Other immunoglobulins may also potentiate HIT.

HIT exists in two forms. A benign form of HIT, type I, is observed in approximately 10% to 20% of patients receiving unfractionated heparin. This mild form of thrombocytopenia (rarely less than 100,000 per μL) occurs after 1 to 4 days of therapy with heparin. It is due to proaggregatory effects of heparin on platelets and generally improves despite continuing heparin administration. In contrast, HIT type II is a life-threatening condition that develops 5 to 10 days after initiating heparin therapy

and is associated with devastating thromboembolic processes (most commonly arterial thrombosis resulting in limb ischemia, cerebrovascular events, and myocardial infarction), from activated platelets that adhere, aggregate, and form platelet ("white") clots. The platelet count falls to less than 50,000 per μL and in severe cases to less than 5,000 per μL. The incidence of HIT in patients receiving full-dose heparin ranges between 0% and 30%. Although there is no randomized prospective study looking at the true incidence of HIT, the expected incidence is estimated to be less than 5%. Those patients who have had a previous exposure to heparin (recent and in some cases remote history) *may* develop HIT earlier after institution of heparin therapy compared with those with no previous exposure. The frequency of HIT is also higher in patients receiving porcine mucosal heparin compared with bovine lung heparin.

The diagnosis of HIT should be entertained in any patient with a significant fall in platelet count while on heparin therapy (less than 150,000 per μL or a 50% or greater decrease in platelet count after 5 days of heparin therapy). The definitive diagnosis requires the following steps: (1) thrombocytopenia while on heparin, (2) exclusion of other etiology of thrombocytopenia, (3) improvement in platelet count following cessation of heparin therapy, and (4) presence of heparin-dependent platelet antibody by an in vitro test. In most cases, the diagnosis is made on clinical findings.

Gerotziafas GT, Elalamy I, Lecrubier C, et al. The role of platelet factor 4 in platelet aggregation induced by the antibodies implicated in heparin-induced thrombocytopenia. *Blood Coagul Fibrinolysis*. 2001;12:511–520.

O'Shea SI, Sands JJ, Nudo SA, et al. Frequency of anti-heparin-platelet factor 4 antibodies in hemodialysis patients and correlation with recurrent vascular access thrombosis. *Am J Hematol*. 2002;69:72–73.

Spiess BD, Horrow J, Kaplan JA. Transfusion medicine and coagulation disorders. In: Kaplan JA, Reich DL, Savino JS, et al. eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: WB Saunders, 2011:949–984.

Warkentin TE, Greinacher A. Heparin-induced thrombocytopenia and cardiac surgery. *Ann Thorac Surg*. 2003;76:2121–2131.

A.15. What is the therapy for HIT?

Because HIT type II is a potentially lethal condition, the most effective therapy is discontinuation of heparin. The thrombocytopenia should improve progressively. Although tempting, the need for platelet transfusion is discouraged because bleeding occurs infrequently and vascular thrombosis may be potentiated. Several anticoagulants have been recommended for use in HIT, as heparin replacement. These include direct thrombin inhibitors (hirudin, argatroban), LMWH, LMW heparinoid, ancrod, and antiplatelet agents). Most of these agents are not available in the United States; others are under clinical investigation. Hirudin has been extensively used in Europe with demonstrable benefit and safety. LMWH has been shown to have cross reactivity with unfractionated heparin approaching 100% (by C-serotonin release or heparin-induced platelet aggregation assays) and should not be used in the setting of HIT unless there are demonstrable negative cross reactivity assays with standard heparin. Ancrod is a defibrinogenating agent (not available in the United States) extracted from the Malayan pit viper and is immunologically distinct from heparin. It acts by cleaving fibrinopeptide A from fibrinogen, and its activity can be measured by assaying for plasma fibrinogen concentration. Finally, in the setting of HIT, a synthetic analogue of prostacyclin (iloprost—a potent inhibitor of platelet activation) has been used successfully during cardiac surgery to inactivate platelets and prevent further reduction of platelet count.

Cheng-Lai A. Cardiovascular drug highlight: hirudin. *Heart Dis*. 1999;1:41–49.

Deitcher SR, Carman TL. Heparin-induced thrombocytopenia: natural history, diagnosis, and management. *Vasc Med.* 2001;6:113–119.

Koster A, Meyer O, Fischer T, et al. One-year experience with the platelet glycoprotein IIb/IIIa antagonist tirofiban and heparin during cardiopulmonary bypass in patients with heparin-induced thrombocytopenia type II. *J Thorac Cardiovasc Surg.* 2001;122:1254–1255.

Robitaille D, Carrier M, Cartier R, et al. Successful management strategy for mechanical assistance and heart transplantation in patients suffering from heparin-induced thrombocytopenia type II. *J Heart Lung Transplant.* 2001;20:1237–1240.

Spiess BD, Horrow J, Kaplan JA. Transfusion medicine and coagulation disorders. In: Kaplan JA, Reich DL, Savino JS, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: WB Saunders; 2011:949–984.

Warkentin TE, Dunn GL, Cybulsky IJ. Off-pump coronary artery bypass grafting for acute heparin-induced thrombocytopenia. *Ann Thorac Surg.* 2001;72:1730–1732.

A.16. Can HIT be caused by LMWH?

Based on confirmed laboratory tests, the prevalence of HIT is 2% for patients receiving unfractionated heparin. Although LMWHs can also induce thrombocytopenia, they may be acceptable alternatives for patients who develop HIT from unfractionated heparin, but reactivity of the particular LMWH with the patient's platelets should be confirmed in vitro.

Fabris F, Luzzatto G, Stefani PM, et al. Heparin-induced thrombocytopenia [review]. *Haematologica.* 2000;85:72–81.

Kleinschmidt K, Charles R. Pharmacology of low molecular weight heparins. *Emerg Med Clin North Am.* 2001;19:1025–1049.

Shore-Lesserson L. Coagulation monitoring. In: Kaplan JA, Reich DL, Savino JS , et al., eds. *Kaplan's Cardiac Anesthesia.* 6th ed. Philadelphia: WB Saunders; 2011:496–516.

Warkentin TE, Sheppard JA, Horsewood P, et al. Impact of the patient population on the risk for heparin-induced thrombocytopenia. *Blood.* 2000;96:1703–1708.

A.17. What is the mechanism of heparin antagonism by protamine?

Heparin is a large molecule consisting of chains of alternating residues of D-glucosamine and uronic acid. It is highly negatively charged, whereas protamine is mostly positively charged. The two combine irreversibly to form a heparin–protamine complex that does not have the ability to bind to thrombin or factor Xa. Once neutralized, the complex of heparin and protamine is eliminated.

Carr JA, Silverman N. The heparin-protamine interaction. A review. *J Vasc Surg.* 1999; 40:659–666.

Kimmel SE, Sekeres M, Berlin JA, et al. Mortality and adverse events after protamine administration in patients undergoing cardiopulmonary bypass. *Anesth Analg.* 2002;94:1402–1408.

Park KW. Protamine and protamine reactions. *Int Anesthesiol Clin.* 2004;42:135–145.

A.18. What is "heparin rebound"?

The ACT is used to confirm the adequacy of heparin neutralization by protamine. The reappearance of circulating heparin several hours after its neutralization by protamine is called heparin rebound and is usually incriminated for clinical bleeding occurring after

cardiac surgery. The concept of heparin rebound following protamine reversal may be explained by sequestration of heparin in tissues that are poorly perfused (i.e., fat), late release of heparin by endothelial cells, and more rapid clearance of protamine in relation to heparin (because heparin is mobilized back into the circulation, it can inhibit thrombin formation and predispose to post-CPB bleeding). Studies in which 1 mg of protamine is given per 100 units of heparin (total dose) found no evidence of heparin rebound.

Spiess BD, Horrow J, Kaplan JA. Transfusion medicine and coagulation disorders. In: Kaplan JA, Reich DL, Savino JS, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: WB Saunders; 2011:949–984.

Subramaniam P, Skillington P, Tatoulis J. Heparin-rebound in the early postoperative phase following cardiopulmonary bypass. *Aust N Z J Surg*. 1995;65:331–333.

A.19. How does warfarin affect the coagulation system? What is the therapy for reversing its effect?

Warfarin (Coumadin) remains the most commonly used anticoagulant agent in the outpatient setting (atrial fibrillation, prosthetic valves, and devices). Its predominant pharmacodynamic effect is inhibition of synthesis of vitamin K–dependent factors (II, VII, IX, and X) in the liver and its clinical efficacy is monitored by measuring the PT or more specifically, the international normalized ratio (INR). The safe or efficacy levels of either INR or PT is variable because of multiple factors, including hepatic, nutritional, drug interaction, age, and presence of other comorbid conditions. On average, it takes several days of therapy to achieve the desired INR (2 to 4); consequently, administration of LMWH or unfractionated heparin may be necessary for initiating anticoagulation. Complications occur because of inadequate anticoagulation (thrombosis) or because of excessive anticoagulation (bleeding and hemorrhage). To reverse its effect, warfarin should be discontinued several days (more than 3 days) to allow levels of the aforementioned factors to normalize. Acute reversal is achieved with FFP. Administration of vitamin K is often necessary to accelerate the synthetic process.

Jacobs LG. Warfarin pharmacology, clinical management, and evaluation of hemorrhagic risk for the elderly. *Clin Geriatr Med*. 2006;22:17–32, vii-viii.

O'Donnell JM, Nacul FE, eds. *Surgical Intensive Care Medicine*. 2nd ed. New York: Springer. 2010:501.

A.20. What do the following measure: prothrombin time (PT), activated partial thromboplastin time (aPTT), thrombin time, activated clotting time (ACT)?

Prothrombin time

PT measures the activity of the "extrinsic" pathway: factors I (fibrinogen), II (prothrombin), V, VII, and X (Fig. 11.5). Deficiencies of factors V, VII, and X (50% of normal) significantly prolong the PT. The concentrations of fibrinogen and prothrombin required to prolong the PT are much lower. The activity of three of the four vitamin K–dependent factors (II, VII, IX, and X) are measured by the PT. Normal values are less than 12 seconds.

Activated partial thromboplastin time

aPTT measures the activity of the "intrinsic" pathway: factors XII, XI, IX, VIII, V, X, prothrombin, and fibrinogen (Fig. 11.5). The aPTT is prolonged when the concentration of these factors is less than 20% to 30%. Normal values are 25 to 40 seconds.

Thrombin time

Thrombin time measures the conversion of fibrinogen to fibrin by thrombin—the final step in the coagulation cascade (Fig. 11.5). The thrombin time is decreased in the presence of low concentrations of fibrinogen and thrombin. Heparin prolongs the thrombin time, whereas warfarin has little effect. Normal values are less than 10 seconds.

Activated clotting time

ACT measures the overall function of the coagulation system. It is used primarily to measure the adequacy of heparinization during CPB and protamine reversal of heparin following CPB. Prolonged ACTs may be due to heparin, low levels of coagulation factors, or thrombocytopenia. It is not particularly specific for platelet or factor deficiencies. Normal values are 110 to 140 seconds.

Owens CD, Belkin M. Thrombosis and coagulation: operative management of the anticoagulated patient. *Surg Clin North Am.* 2005;85:1179–1189.

Sconce EA, Kamali F. Appraisal of current vitamin K dosing algorithms for the reversal of over-anticoagulation with warfarin: the need for a more tailored dosing regimen. *Eur J Haematol.* 2006;77:457–462.

A.21. How is the anticoagulant effect of LMWH monitored?

There is no evidence that monitoring of LMWH dosage improves the clinical efficacy. In contrast, any overdose increases the risk for hemorrhage. Because the kidneys play a significant role in the elimination of LMWH, therapeutic use of these agents should be monitored with an antifactor Xa assay, especially in patients who have renal insufficiency, are elderly, and have clinical conditions that increase the risk for bleeding.

Boneu B, de Moerloose P. How and when to monitor a patient treated with low molecular weight heparin? *Semin Thromb Hemost.* 2001;27:519–522.

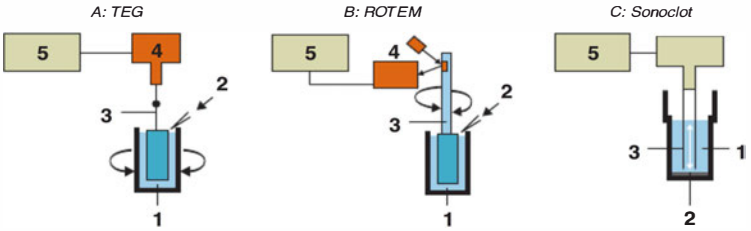
A.22. What is point-of-care testing (POCT) and what are the commonly used point-of-care devices?

The need for POCT has developed as a result of limitations of central laboratories to timely and completely provide results to clinicians for the diagnosis and management of coagulopathic bleeding associated with cardiac surgery, liver transplantation, and trauma beyond standard coagulation tests (PT/aPTT, platelet count, and fibrinogen level). Specific defects in hemostasis (coagulation, analysis of platelet function, as well as abnormal fibrinolysis) can be identified and guided component transfusion practices accomplished. POCT can be performed on-site, in the operating room, and in the ICU. Decrease in the need for blood and blood components (Packed red blood cells, platelets, FFP, cryoprecipitate) has been shown with use of POCT in guiding transfusion practice.

The three devices used in clinical practice are thromboelastography (TEG), rotation thromboelastometry (ROTEM) and Sonoclot analysis.

Thromboelastography (TEG)

The Thromboelastograph (TEG) (Hemoscope Corporation, Niles, IL) measures physical properties of a clot using a stationary cylindrical cup that holds the blood sample and oscillates at an angle. A pin is suspended in the blood by a torsion wire. Motion of the torsion wire is monitored in different phases of in vitro platelet and clot interaction, fibrin formation, and lysis (Fig.11.6A). The analysis performed provides a



A. Thrombelastograph (TEG): Rotating cup with blood sample (1), coagulation activator (2), pin and torsion wire (3), electromechanical transducer (4), data processing (5).

B. Rotation thrombelastography (ROTEM): Cuvette with blood (1), activator added by pipetting (2), pin and rotating axis (3), electromechanical signal detection via light source and mirror mounted on axis (4), data processing (5).

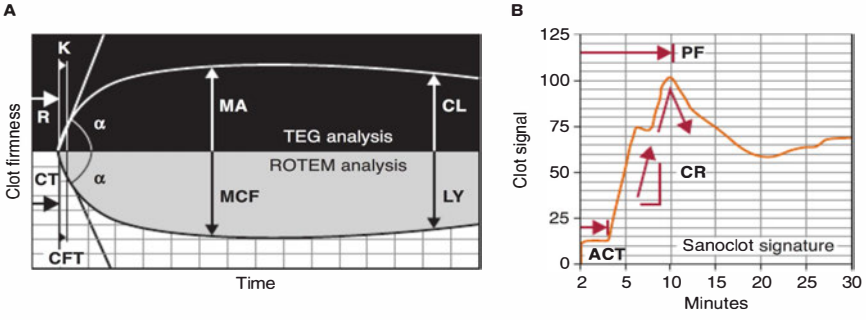
C. Sonoclot: Blood sample in cuvette (1), containing activator (2), disposable plastic probe (3), oscillating in blood sample mounted on electromechanical transducer head (4), data processing (5).

Figure 11.6 Working principles of viscoelastic point-of-care coagulation devices.

graphic and numerical display (Fig.11.7A, upper side). The etiology of a coagulopathy may be obtained by analyzing characteristic TEG signatures (Fig.11.8).

Thromboelastometry

Thromboelastometry also measures viscoelastic properties of a blood sample. ROTEM-rotation thromboelastometry (Pentapharm GmbH, Munich, Germany) is the commercially available device. The principle of the ROTEM is based on the use of a moving pin suspended in a cup of blood sample. The signal is transmitted by an optical detector



A. Upper side:
Thrombelastograph (TEG) tracing: R, reaction time; K, kinetics; α, slope between R and K; MA, maximum amplitude; CL, clot lysis.

A. Lower side:
Rotation thrombelastography (ROTEM) tracing: CT, clotting time; CFT, clot formation time; α, slope of tangent at 2-mm amplitude; MCF, maximal clot firmness; LY, Lysis.

B. Sonoclot signature:
ACT, activated clotting time; CR, clot rate; PF, platelet function.

Figure 11.7 Typical tracings of viscoelastic point-of-care coagulation devices.

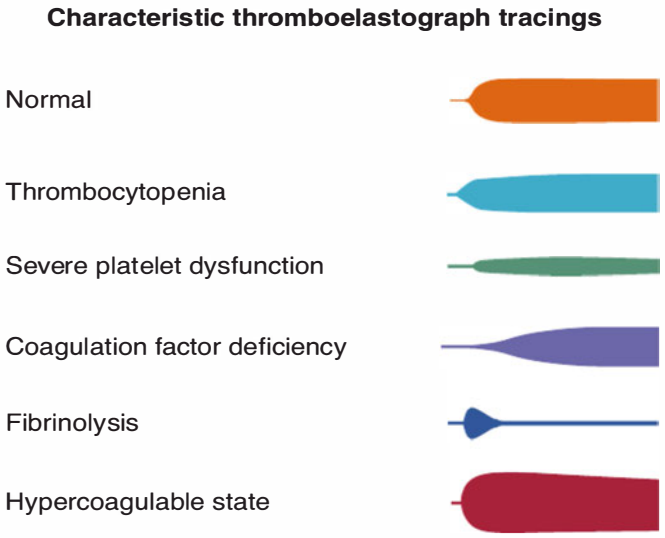


Figure 11.8 Qualitative analysis of thromboelastogram.

system from the moving pin (Fig. 11.6B). The ROTEM provides a measure and graphical display of the changes in viscoelasticity recorded at all stages of the developing clot and characteristic tracings of abnormal findings (Fig. 11.7A lower side and Fig.11.9). Although the basic principles of function as well as the TEG and ROTEM tracings are very similar, the nomenclature and reference ranges are different (Table 11.1).

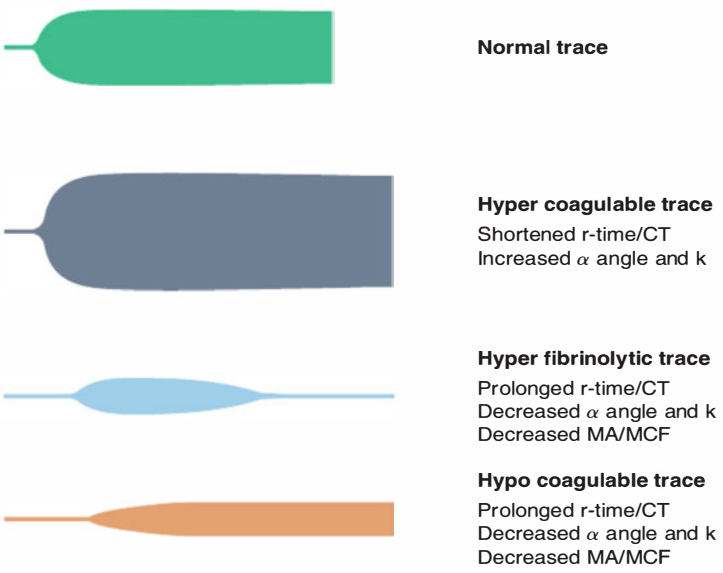


Figure 11.9 Examples of abnormal ROTEM traces.

Table 11.1 Nomenclature and Reference Values of Thrombelastography (TEG) Thrombelastometry (ROTEM)

	TEG	ROTEM®
Clotting time (period to 2 mm amplitude)	*R* (reaction time)	*CT* (clotting time)
	N (WB) 4–8 min	*N* (Cit, in-TEM) 137–246 s
	N (Cit, kaolin) 3–8 min	*N* (Cit, ex-TEM) 42–74 s
Clot kinetics (period from 2 to 20 mm amplitude)	*K* (kinetics)	*CFT* (clot formation time)
	N (WB) 1–4 min	*N* (Cit, in-TEM) 40–100 s
	N (Cit, kaolin) 1–3 min	*N* (Cit, ex-TEM) 46–148 s
Clot strengthening (alpha angle)	α (slope between r and k)	α (slope of tangent at 2 mm amplitude)
	N (WB) 47°–74°	*N* (Cit, in-TEM) 71°–82°
	N (Cit, kaolin) 55°–78°	*N* (Cit, ex-TEM) 63°–81°
Amplitude (at set time)	*A*	*A*
Maximum strength	*MA* (maximum amplitude)	*MCF* (maximum clot firmness)
	N (WB) 55–73 mm	*N* (Cit, in-TEM) 52–72
	N (Cit, kaolin) 51–69 mm	*N* (Cit, ex-TEM) 49–71 mm
		N (Cit, fib-TEM) 9–25 mm
Lysis (at fixed time)	CL30, CL60	LY30, LY60

TEG: *N* = normal values for kaolin activated TEG in native whole blood (WB) or citrated and recalcified blood samples (Cit) (Haemoscope Corp.). ROTEM: *N* = normal values for contact (partial thromboplastin phospholipids, in-TEM), tissue factor (ex-TEM), and tissue factor plus platelet inhibitor cytochalasin D (fib-TEM) activated, citrated, and recalcified blood samples.[6] Reference values depend on reference population, blood sampling technique, other preanalytical factors, and coagulation activator.

Abnormal ROTEM tracing's reflective of specific defects of hemostasis are illustrated in Fig. 11.9

Sonoclot analyzer

The Sonoclot similarly measures the development of clot viscoelastic strength. The principle of function is based on a vertically moving piston (Fig. 11.6C). The device measures the impedance to vibration at the tip of the probe. Information provided includes function of coagulation, fibrin gel formation, clot retraction (platelet function) and fibrinolysis. The Sonoclot analyzer generates both a qualitative graph (Sonoclot signature) and quantitative results on the clot formation time (ACT—onset) and rate of fibrin polymerization (clot rate) (Fig. 11.7B).

Ganter MT, Hofer CK. Coagulation monitoring: current techniques and clinical use of viscoelastic point of care coagulation devices. *Anesth Analg.* 2008;1366–1375.

Luddington RJ. Thromboelastography/thromboelastometry. *Clin Lab Haem.* 2005;27:81–90.

Shore-Lesserson L. Coagulation monitoring. In: Kaplan JA, Reich DL, Lake CL, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: WB Saunders; 2011:496–516.

Vig S, Chitolie A, Bevan DH, et al. Thromboelastography: a reliable test? *Blood Coagul Fibrinolysis.* 2001;12:555–561.

A.23. How does desmopressin aid hemostasis?

Desmopressin (1-deamino-8-D-arginine vasopressin [DDAVP]) is a vasopressin analog with more potency, longer lasting antidiuretic activity, and much less vasoconstriction than the parent compound. Desmopressin increases von Willebrand's factor and factor VII activity in plasma. von Willebrand's factor is found in subendothelial tissue, is released from platelets, and is in part responsible for platelet adhesion to damaged blood vessels. DDAVP was initially shown to significantly decrease postoperative bleeding. Although its routine use is not recommended, DDAVP may be beneficial in patients with end-stage renal disease to increase von Willebrand's factor that is decreased in those patients. The optimal dose of DDAVP is 0.3 μg per kg.

Kondo NI, Maddi R, Ewenstein BM, et al. Anticoagulation and hemostasis in cardiac surgical patients. *J Card Surg*. 1994;9:443–461.

Spiess BD, Horrow J, Kaplan JA. Transfusion medicine and coagulation disorders. In: Kaplan JA, Reich DL, Savino JS, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: WB Saunders; 2011:949–984.

A.24. What is fibrinolysis?

Fibrinolysis is fibrin breakdown in thrombi. Plasmin, derived from plasminogen, is the enzyme involved in this process. Physiologic fibrinolysis involves clot remodeling and removal during the healing process. Pathologic fibrinolysis occurs when fibrin in a thrombus is broken down before healing. Although elevated concentrations of plasminogen activators are found during CPB, their half-lives are very short after bypass.

Spiess BD, Horrow J, Kaplan JA. Transfusion medicine and coagulation disorders. In: Kaplan JA, Reich DL, Savino JS, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: WB Saunders; 2011:949–984.

A.25. What is aminocaproic acid? What is tranexamic acid?

ϵ-Aminocaproic acid (Amicar) and tranexamic acid are analogues of lysine. Their primary mechanism of action is inhibition of plasminogen and plasmin, resulting in less breakdown of fibrinogen, fibrin (fibrinolysis), and other clotting components. These antifibrinolytic agents have been effective in treating coagulopathy in the setting of heart surgery, portocaval shunts, hematologic disorders such as aplastic anemia, abruptio placentae, hepatic cirrhosis, and neoplastic diseases.

Compared with placebo, use of tranexamic acid or aminocaproic acid in cardiac surgery has been shown to reduce blood loss by 30% to 49% as well as reduce homologous blood transfusion. Considering the low cost associated with aminocaproic acid therapy (less than $12), many cardiac surgical centers use this agent routinely for uncomplicated open-heart procedures.

The standard intravenous preparation and dosage for cardiac surgery include 5 to 10 g of aminocaproic acid diluted and infused over 1 hour, followed by a continuous infusion at a rate of 1 g per hour. Higher infusion rates may be used. There are several adverse events that include thrombosis (early graft closure, myocardial ischemia, and infarction), agranulocytosis, leukopenia, and thrombocytopenia. Although rare, bradycardia and mild reduction in blood pressure have also been reported.

Levi M, Cromheecke ME, de Jonge E, et al. Pharmacological strategies to decrease excessive blood loss in cardiac surgery: a meta-analysis of clinically relevant endpoints. *Lancet*. 1999;354:1940–1947.

Spiess BD, Horrow J, Kaplan JA. Transfusion medicine and coagulation disorders. In: Kaplan JA, Reich DL, Savino JS, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: WB Saunders; 2011:949–984.

B. Preoperative Evaluation and Preparation

B.1. Interpret the hemodynamic findings of this patient.

The patient has an adequate blood pressure; however, this appears to be maintained through compensatory mechanisms, including an increase in both arterial resistance (systemic vascular resistance) and HR. The PA systolic pressure is consistent with pulmonary hypertension arising most likely from either chronic mitral valvular disease (stenosis or insufficiency) or decreased compliance of the left ventricle (because it may occur in ischemia). Both the PAD and the PAOP suggest that the left ventricular end-diastolic pressure—a correlate of left ventricular preload—is within the normal limits. Keep in mind that pressure measurements do not correlate with volume status unless the compliance of the chamber (the relation between pressure and volume in diastole) is constant. Therefore, a PAOP of 14 mm Hg could represent hypovolemia, normovolemia, or hypervolemia depending on the compliance of the left ventricle. A CVP of 23 mm Hg is suggestive of right ventricular or biventricular dysfunction, tricuspid stenosis or insufficiency, or obstruction and compression of the right atrium. The CO is inadequate. The derived SV of 22 mL (CO/HR) combined with the other derangements (elevated CVP strongly reflects right heart dysfunction). Taking into consideration the patient's overall presentation (physical examination and laboratory findings), the differential diagnosis includes right ventricular ischemia and/or infarction, pulmonary embolism, atrial or ventricular septal defect causing volume overload of the right ventricle, and cardiac tamponade. An echocardiogram should be performed to assist in the diagnostic process and clinical management.

Fontes ML, Bellows W, Ngo L, et al. McSPI Research Group. Assessment of ventricular function in critically ill patients: limitations of pulmonary artery catheterization. Institutions of the McSPI Research Group. *J Cardiothorac Vasc Anesth*. 1999;13: 521–527

Kern MJ, Lim MJ, Goldstein JA. Hemodynamic rounds: interpretation of cardiac physiology from pressure wave analysis. 3rd ed. Hoboken: Wiley-Blackwell; 2009:269.

B.2. How would you treat the low output status of this patient?

Although the HR is increased, it may be unwise to attempt to normalize it before correcting the SV. The latter is a function of the preload, the afterload, and the contractile status of the myocardium. Whereas the preload of the right heart may be excessive (CVP = 23 mm Hg), the preload of the left heart may not be adequate despite a PAOP of 14 mm Hg. While waiting for the echocardiogram to be performed, a fluid bolus can be attempted. If there is a positive response (i.e., the blood pressure and/or the CO increase), additional fluid bolus can be administered until the limit of the preload reserve has been reached (operating on the flat end portion of the Frank-Starling curve). In the setting of right ventricular failure, it is customary to fluid load the patient. It is important to note that fluid challenge alone will not improve cardiac performance without addressing the contractility and the afterload that, in this patient, appear to be deranged. Because there is no knowledge of the exact etiology of the low output state, it would be rational to institute inotropic support. With regard to the afterload, both systemic and pulmonary afterload are elevated. On the

right side, PA hypertension can be improved with nitroglycerin or nitroprusside but the associated systemic hypotension would prohibit their use. In fact, most vasodilators with the exception of nitric oxide would compromise the systemic pressures. At the same time, if the compliance of the right ventricle is presumed to be decreased, then the increased CVP does not necessarily correlate with adequate preload of the right ventricle. Alternatively, an inotrope that has vasodilatory properties, such as milrinone or dobutamine, would be a better choice. In summary, a rational management of the hemodynamic findings presented would include administering fluid (crystalloid or blood products as indicated), prescribing inotropic support, obtaining an echocardiogram, and addressing the other systemic complications (pulmonary, renal, and coagulation).

Ghobashy A, Fontes ML, Hines RL. Cardiogenic shock. In: Murray MJ, Coursin DB, Pearl RG, et al., eds. *Critical Care Medicine: Perioperative Management*. 2nd ed. Philadelphia: Lippincott Williams & Wilkins; 2002:287.

Levy JH, Tanaka K, Bailey JM, et al. Postoperative cardiovascular management. In: Kaplan JA, Reich DL, Savino JS, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: WB Saunders; 2011:1025–1045.

B.3. How would you evaluate this patient's coagulation status?

A complete blood cell count and a complete coagulation panel should be performed. Assuming that both the hematocrit and the platelet function are adequate, attention should be directed to the elevated PT and the aPTT. The patient has a prosthetic valve and it would be appropriate to surmise that she has been taking anticoagulants. The most common agent to be used 4 days after surgery is warfarin (Coumadin). Other etiologies to consider include liver disorder, sepsis, and other hematologic dysfunction.

Keller C, Matzdorff AC, Kemkes-Matthes B. Pharmacology of warfarin and clinical implication. *Semin Thromb Hemost*. 1999;25:13–16.

Spiess BD, Horrow J, Kaplan JA. Transfusion medicine and coagulation disorders. In: Kaplan JA, Reich DL, Savino JS, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: WB Saunders; 2011:949–984.

B.4. What do fresh frozen plasma (FFP) and cryoprecipitate contain?

FFP contains the labile factors V and VIII as well as the stable coagulation factors (II, VII, IX, X, XI). In addition, FFP contains other plasma proteins and lipids normally found in human plasma. Cryoprecipitate is derived by thawing FFP at 4° C (39.2° F). It contains factors VIII and XIII, von Willebrand's factor, and fibrinogen.

Drummond JC, Petrovich CT. Hemotherapy and hemostasis. In: Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2006:221.

B.5. What are the indications for transfusing FFP, platelet concentrate, and cryoprecipitate?

Blood usually coagulates appropriately when coagulation factor concentrations are at least 20% to 30% of normal and when fibrinogen levels are greater than 75 mg per dL. Although laboratory values such as PT and PTT may be abnormal, the American Society of Anesthesiologist Task Force on Blood Component Therapy

discourages conventional use of FFP for perioperative treatment of bleeding because there are few clinical circumstances whereby coagulopathy arises from factor deficiency. Although massive blood replacement can produce prolongation of PT and/or PTT, the task force states that a true dilutional coagulopathy does not ordinarily occur until more than 100% of the patient's blood volume has been replaced. It supports the use of FFP in patients having vascular bleeding with PT and PTT values greater than 1.5 times the laboratory's normal value. FFP should be administrated in doses calculated to achieve a minimum of 30% of plasma factor concentration (i.e., 10 to 15 mL per kg of FFP).

Recommended indications for FFP:

- Replacement of factor deficiencies
- Reversal of warfarin effect
- Massive blood transfusions
- Treatment of antithrombin III deficiency in patients who are heparin resistant requiring systemic anticoagulation with heparin

In 1994, the College of American Pathologists recommended platelet transfusions after CPB in patients with normal coagulation values and platelet count below 100,000 per μL when major unexplained bleeding occurs. Transfusion of one platelet concentrate will increase the platelet count by approximately 5,000 to 10,000 per μL in the average adult. The usual therapeutic dose is one platelet concentrate per 10-kg body weight.

Platelet concentrate is indicated in the following:

- Active bleeding associated with thrombocytopenia
- Massive blood transfusions

The American Society of Anesthesiologist's Task Force on Blood Component Therapy recommends the administration of cryoprecipitate for:

- Prophylaxis in nonbleeding perioperative or peripartum patients with congenital fibrinogen deficiencies or von Willebrand disease unresponsive to DDAVP (whenever possible, these decisions should be made in consultation with the patient's hematologist)
- Bleeding patients with von Willebrand disease
- Correction of microvascular bleeding in massively transfused patients with fibrinogen concentrations less than 80 to 100 mg per dL

One unit of cryoprecipitate per 10-kg body weight raises plasma fibrinogen concentration approximately 50 mg per dL in the absence of continued consumption or massive bleeding. Bleeding following cardiac surgery without demonstrable abnormalities of coagulation is not considered to be an indication for transfusion of FFP, platelets, or cryoprecipitate. Recent report suggests that postoperative bleeding after CPB may be secondary to excessive fibrinolysis that is responsive to cryoprecipitate. Importantly, the smaller volume of cryoprecipitate compared to FFP makes it a more desirable choice when there is concern of either hemodilution or volume overload.

Kakkar N, Kaur R, Dhanoa J. Improvement in fresh frozen plasma transfusion practice: results of an outcome audit. *Transfus Med*. 2004;14:231–235.

Napolitano LM. Current status of blood component therapy in surgical critical care. *Curr Opin Crit Care*. 2004;10:311–317.

Nuttall GA, Stehling LC, Beighley CM, et al. American Society of Anesthesiologists Committee on Transfusion Medicine. Current transfusion practices of members of the American Society of Anesthesiologists: a survey. *Anesthesiology*. 2003;99:1433–1443.

B.6. What are the complications associated with blood component transfusions?

Complications associated with transfusions of blood elements include transmission of infectious agents (e.g., hepatitis, HIV infection), hemolytic and nonhemolytic transfusion reactions, immunosuppression, anaphylactic or anaphylactoid reactions, and alloimmunization to platelet-specific antigens and the Rh antigen (resulting from erythrocyte contamination because they are stored at room temperature). Platelets in particular may contain proliferating bacteria. Finally, in the immunosuppressed, graft-versus-host effects may occur following platelet transfusion.

Ford SA, Kam PC, Baldo BA, et al. Anaphylactic or anaphylactoid reactions in patients undergoing cardiac surgery. *J Cardiothorac Vasc Anesth*. 2001;15:684–688.

Frère MC, Rapaille A, Bouillenne C, et al. Analysis of 516 reports of reactions after the transfusion of labile blood products. *Transfus Clin Biol*. 2001;8:333–342.

Lacritz EM, Satten GA, Aberle-Grasse J, et al. Estimated risk of transmission of the human immunodeficiency virus by screened blood in the United States. *N Engl J Med*. 1995;333:1721–1725.

Nightingale SD. Department of Health and Human Services Advisory Committee on Blood Safety and Availability. Universal WBC reduction. *Transfusion*. 2001;41:1306–1309.

B.7. What is the risk for acquiring HIV from blood exposure?

The risk for HIV infection in the United States is 1/1,500,000 to 1/2,000,000 per unit transfused. However, with the implementation of donor screening tests for HIV-1 antigen, there is an expectation of preventing up to 25% of the window period cases (the period between viral infection and its detection by tests for the presence of antibodies). Perhaps the immunoviral agent most transmitted by blood transfusion is cytomegalovirus.

Drummond JC, Petrovich CT. Hemotherapy and hemostasis. In: Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:371.

Goodnough LT, Brecher ME, Kanter MH, et al. Transfusion medicine: first of 2 parts—blood transfusion. *N Engl J Med*. 1999;340:438–447.

Napolitano LM. Current status of blood component therapy in surgical critical care. *Curr Opin Crit Care*. 2004;10:311–317.

Reine NJ. Infection and blood transfusion: a guide to donor screening. *Clin Tech Small Anim Pract*. 2004;19:68–74.

B.8. Assuming that the patient has cardiac tamponade, how would you prepare this patient for surgery?

As with any patient undergoing surgery, the following steps should be taken: first, a complete review of the patient's history, physical examination, and laboratory findings are mandated; second, key areas of concern should be identified and appropriate steps taken to address them; third, an anesthetic plan that is tailored to cardiac tamponade is devised; last, communication with the respective medical (surgeons, nurses, perfusionist, blood bank) and paramedical staff to ensure readiness and teamwork. The patient's presentation suggests that she is in some degree of respiratory distress. Initially, management should consist of supplemental oxygen, review of

chest radiograph, and assessment of arterial blood gasses. Shortness of breath and the inability to lie supine are frequent symptoms in patients having cardiac tamponade physiology, and every effort should be made to provide comfort and lessen the associated emotional stress. Positive pressure ventilation should be avoided at all cost unless the clinical picture indicates that the patient will have a cardiac arrest. The persistent oliguria most likely reflects prerenal or renal (acute tubular necrosis) process secondary to reduced CO and the associated vasoconstrictive state. As described in the previous answer, optimization of hemodynamics should also improve the renal function. Whereas some may administer diuretics in this setting, such management is strongly discouraged. The most effective management is surgical evacuation of the PE or clot. The hematologic issues include elevated PT and aPTT, blood loss, and the potential for further blood loss perioperatively. The coagulopathy should be corrected appropriately, the patient's hematocrit and platelets should be checked and treated accordingly, and sufficient blood (4 to 6 units) will be required in the operating room before commencing surgery.

Ghobashy A, Fontes ML, Hines RL. Cardiogenic shock. In: Murray MJ, Coursin DB, Pearl RG, et al., eds. *Critical Care Medicine: Perioperative Management*. 2nd ed. Philadelphia: Lippincott Williams & Wilkins; 2002:287.

Levy JH, Tanaka K, Bailey JM, et al. Postoperative cardiovascular management. In: Kaplan JA, Reich DL, Savino JS, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: WB Saunders; 2011:1025–1045.

C. Intraoperative Management

C.1. How would you monitor this patient during transport to the operating room? What emergency drugs would you bring with you?

The patient must be under astute observation, and the vital signs must be continuously assessed, including invasive monitoring of systemic blood pressure, electrocardiogram, and oxygen saturation. In addition, emergency cardioactive and vasoactive drugs should be available during transport:

- Oxygen: Increase the F_{IO_2} as needed. All necessary equipment for intubation should be present (laryngoscope and several blades, bag-mask units, and adult-size endotracheal tubes)
- DC cardioversion unit: in case of tachyarrhythmias
- Phenylephrine: dose: bolus, 0.1 to 0.5 mg; infusion, 25 to 125 μg per minute
- Epinephrine: dose: 0.01 to 0.1 μg/kg/minute
- Calcium chloride: dose: 2 to 4 mg per kg
- Lidocaine: 1 to 2 mg per kg
- Atropine: 0.01 mg per kg

C.2. In this patient, what hemodynamic effects would occur from intravenous induction with ketamine, thiopental, fentanyl, propofol, etomidate, or midazolam?

Ketamine

After intravenous administration, ketamine (1 mg per kg) has a rapid onset of action and achieves a peak plasma concentration in less than 1 minute. It also possesses a short duration of action. After the initial dose, patients may remain unconscious for 10 to 15 minutes, but the analgesic effect (somatic greater than visceral) persists for an additional 30 minutes or longer. Some of the hemodynamic effects of ketamine may

include small increases in blood pressure, HR, CO, and myocardial oxygen demand. This response is mediated by a direct central sympathetic stimulation and by inhibition of norepinephrine uptake into the postganglionic sympathetic nerve endings. Ketamine has also been shown to have intrinsic depressant properties on the myocardium. In clinical conditions in which norepinephrine stores are reduced, and in the presence of pre-existing cardiac dysfunction (mechanical or myocardial), administration of ketamine can produce hemodynamic depression.

Fentanyl

Fentanyl does not possess any depressant effects on myocardial contractility but because of its vagotonic effect (decreases in HR) and mild sympatholytic effect (central sympathetic outflow), blood pressure may decrease. This response may be more profound in shock or preshock states, and when fentanyl is used concomitantly with other induction agents (benzodiazepines, thiopental, propofol).

Propofol

Propofol produces effects very similar to those of thiopental. It can cause significant reduction in systemic pressures (greater than 30%), and there have been several reports of cardiovascular arrest in both adults and children following inductions with propofol. Propofol also has some antiarrhythmic effect on the atrioventricular node, as well as on other conduction pathways. It should be used with caution when other agents that slow down atrioventricular nodal conduction are present (calcium channel blockers, β-blockers, digoxin). As with thiopental, the use of propofol for induction in cardiac tamponade is strongly disfavored.

Etomidate

Etomidate has a very favorable hemodynamic profile and is the preferred agent to be used during induction when cardiovascular collapse is anticipated. With an induction dose (0.2 to 0.3 mg per kg), etomidate may cause a slight decrease in mean arterial pressure but such changes are not attributable to myocardial depression, as is typical of propofol and sodium thiopental. Pain at the injection site and involuntary muscle movements are the most common adverse events noted with etomidate. It also appears to reduce seizure threshold and enhance its duration when used during electroconvulsion therapy.

Midazolam

Midazolam may cause mild to moderate systemic vasodilation, particularly when used in combination with opioids.

Overall, of the agents discussed, etomidate would be the preferred agent for induction, followed by ketamine, and/or fentanyl; thiopental and propofol would be the least desired.

White PF, Romero G. Nonopioid intravenous anesthesia. In: Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:450–455.

C.3. Describe the induction process for cardiac tamponade.

The patient should have standard monitors placed, as well as invasive monitors, including indwelling arterial access for beat-to-beat monitoring of systemic arterial pressures and for obtaining blood gases. This patient has a PAC in situ; however, its usefulness in this setting remains debatable. The actual induction should proceed ONLY in the presence of a surgical team that is ready and gowned and after the patient has been completely prepared and draped. The choice of induction agents is limited to opioids,

muscle relaxant (depolarizing or nondepolarizing), and either etomidate or ketamine. Regardless of the induction technique, the anesthesiologist should expect, and be prepared to manage, ensuing circulatory collapse.

Levy JH, Tanaka K, Bailey JM, et al. Postoperative cardiovascular management. In: Kaplan JA, Reich DL, Savino JS, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: WB Saunders; 2011:1025–1045.

C.4. Following induction and intubation, the systemic blood pressure decreased to 55/30 mm Hg. Describe the clinical events accounting for this perturbation and the management steps required for resuscitation.

Cardiac tamponade is caused by significant pericardial pressure from accumulating pericardial contents (fluid, blood, and blood clots) that impede chamber filing resulting in a low CO state. The precipitous fall in blood pressure observed with induction can be accounted for by the following: first, most induction agents will have negative hemodynamic effects that are either direct or indirect; second, sympatholysis reduces arterial resistance as well as chronotropy and inotropy of the heart; third, the physiologic consequences of switching from negative pressure ventilation to positive pressure ventilation will further reduce cardiac filling by increasing intrathoracic pressure and afterload; and finally, placing the patient in a supine position will also compromise atrial and ventricular preload (i.e., hydrostatic effects, loss of diaphragmatic motion, and mediastinal structures weighing on the heart).

The management of hypotension will require use of vasoactive drugs, cardioactive drugs, and/or fluid challenge. Reducing inspiratory positive pressure (i.e., lowering tidal volume or switching from ventilator-delivered breaths to hand ventilation) may also improve the hemodynamic status by facilitating filling. These would be merely temporizing measures; surgical relief of tamponade would be the definitive treatment of this problem.

Levy JH, Tanaka K, Bailey JM, et al. Postoperative cardiovascular management. In: Kaplan JA, Reich DL, Savino JS, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: WB Saunders; 2011:1025–1045.

C.5. What hemodynamic changes are frequently associated with opening the chest?

Chest opening normalizes the pressure relation between the pericardium and the heart chambers, thereby relieving the tamponade and its hemodynamic effects. Unless the myocardium has suffered injury or is stunned, the expected hemodynamic changes include drastic improvement in both blood pressure and SV. Most of the vasoactive and cardioactive agents being administered can be quickly weaned. In addition, oxygenation, acid–base status, and renal function (urine output) tend to improve significantly.

C.6. What is myocardial stunning? What is myocardial hibernation?

The myocardium can exhibit segmental dysfunction or a generalized decrease in function related to injury (i.e., ischemia and infarction). It has also been noted that myocardial function can be coupled or uncoupled with tissue perfusion. For example, following a period of oxygen deprivation and restoration of flow, the affected myocardium can resume normal function, or have diminished function or no function

(dysfunction). The term *myocardial stunning* represents a state of uncoupling between function and flow in which myocardial flow is normal but function is diminished or absent. In the setting of cardiac surgery, myocardial stunning can be a cause of ventricular dysfunction that generally resolves within the first 6 to 8 hours post-CPB. During this period, inotropic support has been shown to be effective. Myocardial hibernation, on the other hand, is a myocardial process that manifests after weeks or months and denotes a condition in which both myocardial function and flow are reduced (perfusion and function are coupled). Perhaps this is an adaptive process that allows the myocytes to lower their metabolic activity and oxygen consumption to survive during states of oxygen deprivation. The definitive diagnosis of stunning and hibernation may be difficult to make because regional myocardial blood flow is difficult to assess or quantify clinically. Therefore, most cases of stunning and hibernation require a retrospective analysis. First, segmental myocardial dysfunction must be established; second, myocardial blood flow should be restored by revascularization (surgical, pharmacologic, or angioplasty/stenting); and third, improvement of regional function should follow revascularization.

D'Ancona G, Donias HW, Bergsland J, et al. Myocardial stunning after off-pump coronary artery bypass grafting: safeguards and pitfalls. *Ann Thorac Surg*. 2001;72:2182–2183.

Grocott HP, Stafford-Smith M. Organ protection during cardiopulmonary bypass. In: Kaplan JA, Reich DL, Savino JS, et al., eds. *Kaplan's Cardiac Anesthesia*. 6th ed. Philadelphia: WB Saunders; 2011:838–887.

Shah BR, Velazquez E, Shaw LK, et al. Revascularization improves survival in ischemic cardiomyopathy regardless of electrocardiographic criteria for prior small-to-medium myocardial infarcts. *Am Heart J*. 2002;143:111–117.

Watzinger N, Saeed M, Wendland MF, et al. Myocardial viability: magnetic resonance assessment of functional reserve and tissue characterization. *J Cardiovasc Magn Reson*. 2001;3:195–208.

D. Postoperative Management

D.1. How would you manage hypertension in the intensive care unit (ICU)?

The management of hypertension depends on its etiology. Rather than administering antihypertensive agents indiscriminately, the clinician should exclude the following conditions as causality of hypertension: hypoxemia, hypercarbia, acid–base derangements, and pain. The occurrence of hypertension is a common phenomenon during the first several hours in the ICU. In most cases, the etiology is uncertain and probably represents a state of marked sympathoadrenal activation. Once correctable causes of hypertension have been addressed, antihypertensive therapy can be achieved with a variety of agents. Because the underlying mechanism of the hypertension involves endogenous release of norepinephrine (with minimal epinephrine), the most rational agents to use are the β-blockers. Labetalol antagonizes both α- and β-adrenergic receptors and is an effective antihypertensive agent. Alternatively, metoprolol, atenolol, esmolol, or propranolol can be used, particularly if the hypertension is associated with tachycardia. Unfortunately, these agents are used infrequently because of theoretical concerns of myocardial depression and bradycardia. Current cardiology practice strongly endorses the use of β-blockers in the setting of moderate and severe ventricular dysfunction. In addition, the cardioprotective effects of β-blockers have been shown in several perioperative trials whereby the incidence of myocardial injury and mortality (up to 2 years postoperatively) are significantly reduced in patients treated perioperatively with β-blockers.

Kotlyar E, Macdonald PS, Keogh AM, et al. Optimization of left ventricular function with carvedilol before high-risk cardiac surgery. *J Heart Lung Transplant*. 2001;20:1129–1131.

Varon J, Marik PE. Perioperative hypertension management. *Vasc Health Risk Manag*. 2008;4:615–627.

D.2. When would it be appropriate to extubate this patient?

The timing of extubation depends on the following:

- Clinical stability (stable hemodynamics without need for significant inotropic or vasoactive support)
- Intact neurologic function (alertness and ability to comprehend and execute simple verbal commands)
- Adequate pulmonary function (acceptable arterial blood gases and acid–base status and adequate weaning parameters—tidal volume, respiratory rate, vital capacity, and inspiratory effort)
- Normal body temperature and neuromuscular function (reverse paralysis if necessary)
- Normal coagulation (bleeding less than 60 mL per hour and normalization of coagulation parameters)

Following relief of tamponade, most patients can be extubated as early as possible assuming that the previously listed criteria have been met.

CHAPTER 12

Heart Transplantation and Subsequent Noncardiac Surgery

Jeff T. Granton and Davy C. H. Cheng

A 41-YEAR-OLD MAN

with a history of idiopathic dilated cardiomyopathy is admitted to the cardiac care unit in a quaternary cardiac center for potential heart transplantation assessment. He has known systolic dysfunction, with an ejection fraction of <25% on transthoracic echocardiogram. Recurrent ventricular arrhythmias necessitated insertion of an implantable cardioverter defibrillator (ICD). Right heart catheterization revealed a pulmonary vascular resistance (PVR) of 4 Woods units. Recently, his symptoms have worsened and have progressed to New York Heart Association class IV. During this hospital admission, his clinical status continued to deteriorate, necessitating the initiation of inotropic support and the insertion of an intra-aortic balloon pump (IABP). He is subsequently placed on the transplant list with high priority. However, due to further deterioration, consideration is being given to the insertion of a left ventricular assist device (VAD) to maintain adequate end-organ perfusion while waiting for a donor heart to become available.

A. Medical Disease and Differential Diagnosis

1. What are the common diagnoses requiring adult heart transplantation?
2. What are the indications and relative contraindications for recipient selection?
3. What are the criteria for donor heart selection?
4. What are the principles of perioperative donor management?
5. What are the risk factors associated with posttransplant mortality?
6. What is the difference between the biatrial and bicaval surgical techniques of heart transplant?
7. When is combined heart/lung transplant indicated? What are the important differences?
8. What are the medical and surgical alternatives to cardiac transplantation?
9. What is the role for VADs in these patients?

10. What are the considerations in anesthetizing patients for left ventricular assist device (LVAD) insertion?

B. Preoperative Management

Three weeks after insertion of an LVAD, a donor heart becomes available.

1. How would you assess this patient preoperatively?
2. How would you premedicate this patient? Why?

C. Intraoperative Management

1. What anesthetic equipment and monitors would you set up? Why?
2. What is the role of transesophageal echocardiography (TEE)?
3. Describe the induction and maintenance of anesthesia.
4. How would you manage this patient during cardiopulmonary bypass (CPB)?

D. Postoperative Management

1. What are the early postoperative complications?
2. What are the mechanisms of early right heart failure?
3. How would you treat right heart failure following heart transplantation?
4. How does inhaled nitric oxide (NO) work as a selective pulmonary vasodilator?
5. What is the pathophysiology of the denervated heart?
6. What are the common cardiac dysrhythmias following heart transplant?
7. What are the causes of posttransplant bleeding?
8. How would you treat posttransplant bleeding?
9. What are the causes of early graft failure?
10. How would you manage this patient in the intensive care unit?

E. Subsequent Noncardiac Surgery

The patient recovers successfully following heart transplant. However, 2 years postoperatively, he fractures his left radius after a fall. He then presents for open reduction and internal fixation of the fracture.

1. How would you monitor this patient?
2. What type of anesthetic is best for the heart-transplanted patient?
3. Which anesthetic technique would you give this patient?
4. Do you need to use a muscarinic antagonist with cholinesterase inhibitors to reverse the muscle relaxant in heart-transplanted patients?
5. What are the anesthetic implications for heart-transplanted patients?
6. What is the significant implication of the denervated heart?
7. What is the significance of allograft rejection?
8. What is the significance of infection in these patients?
9. What are the significant implications of drug interactions?
10. What is cardiac allograft vasculopathy (CAV)? Why is this important?
11. What is the significant implication of posttransplant hypertension?
12. What is the significant implication of renal dysfunction?
13. Is ambulatory surgery appropriate for heart transplant recipients?

A. Medical Disease and Differential Diagnosis

A.1. What are the common diagnoses requiring adult heart transplantation?

Heart transplantation is now considered to be a viable treatment option for selected patients with end-stage heart disease. At present, more than 4,000 heart transplants

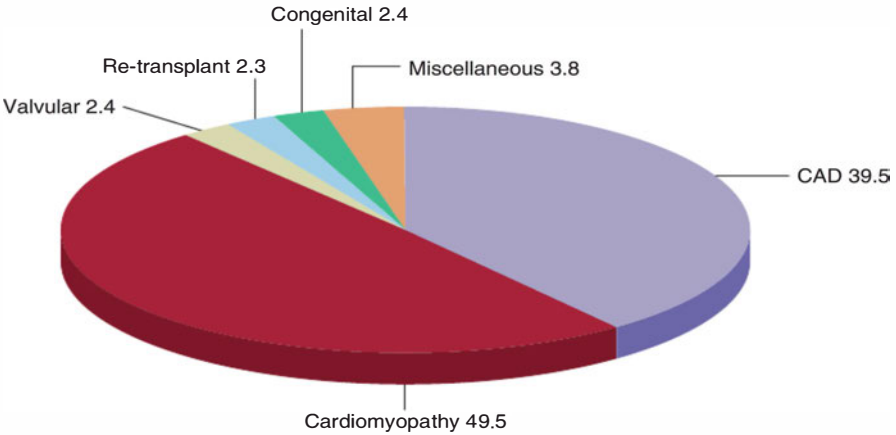


Figure 12.1 Indications for adult heart transplant (%). CAD, coronary artery disease.

are done annually worldwide. The indications for adult heart transplant, as reported to the Registry of the International Society for Heart and Lung Transplantation from 2002 to 2008, are shown in Figure 12.1. Ischemic coronary artery disease (39.5%) and nonischemic cardiomyopathy (49.5%) represent the most frequent causes for transplantation.

Taylor DO, Oz M, Mancini D, et al. Registry of the International Society for Heart and Lung Transplantation: twenty-sixth official adult heart transplant report-2009. *J Heart Lung Transplant*. 2009;28(10):1007–1022.

A.2. What are the indications and relative contraindications for recipient selection?

It should be noted that indications/contraindications can be flexible and can vary from center to center.

Criteria for selection include the following:

- End-stage heart disease
- Physiologic age less than 65. However, over the last 10 years, greater than 20% of heart recipients were ≥60 years of age. There are even rare cases of patients greater than 70 years old receiving a heart transplant.
- Maximal oxygen uptake ($\dot{V}O_{2max}$) during cardiopulmonary exercise testing is considered. Although the cut-offs are highly variable and have many caveats, generally, patients with a peak $\dot{V}O_{2max}$ <10 mL/kg/min have an indication for transplantation.

Contraindications (not necessarily absolute)

- Neoplasm with significant chance of recurrence
- Obesity (BMI >30 kg/m^2)
- Fixed pulmonary hypertension: PVR greater than 5 Woods units
- Nonreversible renal dysfunction
- Age over 70
- Peripheral vascular disease, carotid stenosis (depending on severity)

- Diabetes with end-organ damage neuropathy, nephropathy, retinopathy
- Psychosocial impairments
- Drug or alcohol addiction, smoking, mental defect that will limit compliance, history of noncompliance
- Other diseases that may limit survival (human immunodeficiency virus [HIV], pulmonary disease, hepatitis, etc.)

Merha MR, Kobashigawa J, Starling R, et al. Listin criteria for heart transplantation: International Society for Heart and Lung Transplantation guidelines for the care of cardiac transplant candidates-2006. *J Heart Lung Transplant*. 2006;25(9):1024–1042.

Steinman TI, Becker BN, Frost AE, et al. Guidelines for the referral and management of patients eligible for solid organ transplantation. *Transplantation*. 2001;71:1189–1204.

Taylor DO, Oz M, Mancini D, et al. Registry of the International Society for Heart and Lung Transplantation: twenty-sixth official adult heart transplant report-2009. *J Heart Lung Transplant*. 2009;28(10):1007–1022.

A.3. What are the criteria for donor heart selection?

The limiting factor in heart transplantation is the shortage of donor organs. In Canada, 162 heart transplants were performed in 2008, with 131 people on the waiting list at the end of that year. In the United States, 2,163 heart transplants were performed in 2008, with 2,791 patients on the waiting list as of June 2009. Following establishment of brain death, organ harvest may be considered for the purpose of donation. Preferably, the donor should not have sustained prolonged cardiac arrest, severe chest trauma, intracardiac injections, septicemia, excessive inotropic support, and be less than 55 years of age. In all cases, a careful clinical examination of the potential donor is undertaken to rule out coronary artery atherosclerosis and contractile dysfunction; investigations may include angiography and echocardiography. The use of coronary angiography would be dictated by patient age, sex, and risk factors. In general, a contrast ventriculogram is avoided to reduce the risk of nephrotoxicity.

Poor ejection fraction (<40%), despite optimization of physiologic variables, would exclude a potential donation. Transplantation can proceed with mild left ventricular hypertrophy, however, wall thickness >13 mm or electrocardiogram (ECG) criteria for left ventricular hypertrophy would make transplantation unadvisable. In general, severe congenital or valvular abnormalities would preclude donation, with the exception of abnormalities in which "bench" repair can be undertaken before transplant.

ABO compatibility is important, as mismatch may result in hyperacute rejection. The donor body weight should be within 20% of that of the recipient. However, in the case of a small donor matching, using BMI or height is more accurate than using weight. Preferably donor heart ischemic time should be less than 4 hours. Prolonged ischemic time may contribute to early allograft failure; however, techniques to allow improved tolerance of ischemia may be on the horizon.

The use of non–heart-beating donors is now used in multiple jurisdictions for kidney, liver, and lung transplantation. There have been cases of heart transplantation from non–heart-beating donors. However, the ethical and legal issues surrounding the technique for this form of heart donation are controversial.

Costanzo MR, Task Force. The International Society of Heart and Lung Transplantation guidelines for the care of heart transplant recipients. *J Heart Lung Transplant*. 2010;29:914–956.

Eynon AC, Murphy PG, Smith M. Comment and opinions. Heart transplantation after declaration of death by cardiorespiratory criteria. *J Heart Lung Transplant*. 2009;29: 232–233.

Heart and Stroke Foundation of Canada. Statistics web site, 2010.

Hunt SA, Haddad F. The changing face of heart transplantation. *JACC*. 2008;52:587–598.

Jhaveri R, Tardiff B, Stanley TE III. Anesthesia for heart and heart-lung transplantation. *Anesthesiol Clin N Amer*. 1994;12:729–747.

Livi U, Caforio ALP. Heart donor management and expansion of current donor selection criteria. *J Heart Lung Transplant*. 2000;19:S43–S48.

Lloyd-Jones D, Adams RJ, Brown TM, et al. on behalf of the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2010 update. *Circulation*. 2010;121:e46–e215.

Steinman TI, Becker BN, Frost AE, et al. Guidelines for the referral and management of patients eligible for solid organ transplantation. *Transplantation*. 2001;71:1189–1204.

Zaroff JG, Rosengard BR, Armstrong WR, et al. Consensus conference report. Maximizing use of organs recovered from the cadaver donor: cardiac recommendations. *Circulation*. 2002;106:836–841.

A.4. What are the principles of perioperative donor management?

The goals of management are to maintain euvolemia, achieve relatively normal afterload, and optimize cardiac output (CO) without excessive use of inotropic medications, in particular β-agonists. Unfortunately, the brain-dead patient often can become extraordinarily unstable, and achieving hemodynamic stability can be a challenge. In addition, the treatment modalities to support certain end organs for harvest are often at odds with each other. The onset of diabetes insipidus needs to be considered when excessive urine output (greater than 300 mL/hour) is observed and must be treated promptly with desmopressin (1-deamino-8-D-arginine vusopressin [DDAVP]). As a result of dysfunction of the hypothalamic-pituitary system, it is suggested that hormonal replacement therapy be undertaken in patients with ejection fractions less than 40% or with hemodynamic instability. This includes the use of intravenous (IV) exogenous thyroid therapy, arginine vasopressin, and methylprednisolone. In addition, adequate glycemic control should be achieved.

Shemie SD, Ross H, Pagilarello J, et al. Organ donor management in Canada, recommendations of the forum on medical management to optimize donor organ potential. *CMAJ*. 2006;174(4):S13–S30.

Van Bakel AB, Pitzer S, Drake P, et al. Early hormonal therapy stabilizes hemodynamics during donor procurement. *Transplantation Proceedings*. 2004;36:2573–2578.

Zaroff JG, Rosengard BR, Armstrong WR, et al. Consensus conference report. Maximizing use of organs recovered from the cadaver donor: cardiac recommendations. *Circulation*. 2002;106:836–841.

A.5. What are the risk factors associated with posttransplant mortality?

Overall survival at 1 year is 86%. Having congenital heart disease as the indication for transplant is a powerful predictor of postoperative 1-year mortality. In addition, the requirement of extracorporeal circulatory support, dialysis, female gender, preoperative mechanical ventilation, nonidentical ABO matching, previous blood transfusions, coronary artery disease as the indication for transplant, and being hospitalized immediately before transplant all are risk factors for 1-year mortality. Mortality during the first year is greater than the next 4 years combined, so risk factors associated with 1-year mortality are powerful predictors of 5-year mortality. For those that have survived after 1 year, allograft vasculopathy during the first year posttransplant, diabetes, treatment for rejection in year 1, recipient age, donor age, recipient weight, and transplant center volume are risk factors for 5-year mortality.

The most common causes of death are the following:
Within 30 days posttransplant
- Graft failure, multi-organ failure, non-cytomegalovirus infection (CMV)
From 31 to 365 days posttransplant
- Non-CMV infection, graft failure, acute rejection
After 5 years
- Allograft vasculopathy, late graft failures, malignancies, non-CMV infections

Taylor DO, Oz M, Mancini D, et al. Registry of the International Society for Heart and Lung Transplantation: twenty-sixth official adult heart transplant report-2009. *J Heart Lung Transplant*. 2009;28(10):1007–1022.

A.6. What is the difference between the biatrial and bicaval surgical techniques of heart transplant?

The older biatrial technique involves anastomoses of the recipient and donor atrial cuffs. The bicaval technique maintains the above-left atrial anastomoses, and attempts to maintain cardiac anatomy with separate bicaval anastomoses to the right atrium.

Morgan JA, Edwards NM. Orthotopic cardiac transplantation: comparison of outcome using biatrial, bicaval and total techniques. *J Card Surg*. 2005;20:102–106.

A.7. When is combined heart/lung transplant indicated? What are the important differences?

Congenital cardiac disease is the most common indication for combined heart/lung transplant. Other indications include idiopathic pulmonary hypertension, cystic fibrosis, α1-antitrypsin deficiency and other forms of lung disease, such as emphysema and idiopathic pulmonary fibrosis. The procedure is performed through a transverse thoracotomy incision and the donor heart/lungs are transplanted *en-bloc*. Important postoperative problems include bleeding and reperfusion lung injury, which may require NO or occasionally extracorporeal membrane oxygenation (ECMO). Survival following heart/lung transplant is 64%, 43%, and 28% at 1, 5, and 10 years respectively.

Christie JD, Edwards LB, Aurora P, et al. The Registry of the International Society for Heart and Lung Transplantation: twenty-sixth official adult lung and lung–heart transplantation report-2009. *J Heart Lung Transplant*. 2009;28(10):1031–1049.

A.8. What are the medical and surgical alternatives to cardiac transplantation?

An ongoing worldwide shortage of donor hearts has meant ongoing pressure to manage medically patients with end-stage cardiac failure. Patients need to adhere to strict lifestyle modifications and diet, otherwise any other therapy will have limited usefulness. As heart failure progresses, patients may respond to a variety of medications. Angiotensin-converting enzyme (ACE) inhibitors have been shown to improve symptoms and decrease mortality in patients with heart failure. Angiotensin II receptor blockers also can be considered for patients intolerant of ACE inhibitors. Patients with severe forms of heart failure also may benefit from a low-dose aldosterone antagonist (spironolactone), with attention paid to potential hyperkalemia. Tailored doses of diuretic therapy may offer some symptomatic relief. Beta-blockade with carvedilol, sustained-release metoprolol, or bisoprolol has been shown to reduce the risk of death. In addition, patients with advanced heart failure may reduce their risk of sudden cardiac

death by the insertion of an ICD. Furthermore, ICD implantation can be combined with cardiac resynchronization therapy, which has been shown to improve functional class and survival in advanced heart failure, once patients also have achieved optimal medical management. IABP and, increasingly, VAD implantation or semi-implantable pericorporeal devices also are finding a role in the management of patients as a bridge to transplant, particularly for those presenting in acute decompensated heart failure.

Hunt SA, Antman EM, Smith SC, et al. ACC/AHA 2005 guideline update for the diagnosis and management of chronic heart failure in the adult-Summary article. *Circulation*. 2005;112:1825–1852.

Ramani GV, Uber PA, Mehra MP. Chronic heart failure: contemporary diagnosis and management. *Mayo Clinic Proceedings*. 2010;85:180–195.

A.9. What is the role for VADs in these patients?

In the United States, over 1,000 LVADs were placed from 2006 to 2009. Far fewer right ventricular (RVAD) and biventricular assist devices were inserted. Indications for LVAD insertion included cardiogenic shock (30%), progressive decline (40%), and inotrope dependence (15%). Of those that received an LVAD, 87.3% were listed or were being considered for heart transplant. In general, three major categories of patients considered for VAD have emerged. These include (1) temporary insertion while cardiac function recovers from insult (bridge to recovery); (2) insertion while awaiting transplant or transplant assessment (bridge to transplant); and (3) patients who need long-term support, but are not transplant candidates (destination therapy). Interestingly, for almost 10% of patients, LVAD insertion was considered a destination therapy.

A variety of composite risk scores have been developed to help guide patient selection and predict survival after LVAD implantation. Issues such as aortic valve incompetence and the presence of intracardiac shunts need to be investigated, as these may make LVAD insertion unadvisable. It also would seem that there has been a move toward continuous flow pump technology since 2008 versus the pulsatile pump.

Kirklin JK, Naftel DC, Kormos RL, et al. Second INTERMACS annual report: more than 1000 primary left ventricular assist device implants. *J Heart Lung Transplant*. 2010;29(1):1–10.

Wilson SR, Mudge GH, Stewart GC, et al. Evaluation for a ventricular assist device, selecting the appropriate candidate. *Circulation*. 2009;119:2225–2232.

A.10. What are the considerations in anesthetizing patients for left ventricular assist device (LVAD) insertion?

Significant cardiac abnormalities (e.g., aortic insufficiency, patent foramen ovale) should be identified preoperatively and, if possible, addressed at the time of surgery. These patients may have an ICD in place and if deactivated, placement of external defibrillator pads is advisable. LVADs can be inserted with a sternotomy or a left thoracotomy. Patients are at high risk for significant perioperative blood loss and large-bore IV access is essential and antifibrinolytics often are administered. TEE is mandatory for LVAD insertion to assess for patent foramen ovale, ensure aortic valve competence, confirm proper position of device, assess amount of air in cardiac chambers, guide fluid management, and monitor right ventricular (RV) function. Inadequate right heart function is a potential complication after LVAD insertion and can be treated with phosphodiesterase inhibitors and inhaled NO. Vasopressin and/or norepinephrine may be required to maintain adequate systemic vascular resistance post-CPB. However, caution needs to be exercised with vasoconstrictors, as excessive afterload can impair device function.

Mets B. Anesthesia for left ventricular assist device placement. *J Cardiothorac Vasc Anesth*. 2000;14:316–326.

Nussmeier NA, Probert CB, Hirsch D, et al. Anesthetic management for implantation of the Jarvik 2000™ left ventricular assist system. *Anesth Analg*. 2003:97:964–971.

Tan LH, Cokis C. Anesthesia for implantation of the Jarvik 2000 Flowmaker LVAD. *Anaesth Intensive Care*. 2006;34:746–752.

Williams M, Oz M, Mancini D. Cardiac assist devices for end-stage heart failure. *Heart Disease*. 2001;3:109–115.

B. Preoperative Management

Three weeks after insertion of an LVAD, a donor heart becomes available.

B.1. How would you assess this patient preoperatively?

Prospective transplant candidates usually have been fully preoperatively evaluated by a multidisciplinary team, including cardiology, respirology, and surgery, as well as anesthesia. In case of subsequent deterioration, however, the anesthesiologist should review the recipient's current cardiac status, including medications and level of mechanical support, with particular attention to hemodynamic parameters and reversibility of elevated PVR. Pertinent anesthetic history, concomitant diseases, and fasting status also must be ascertained. Baseline electrolytes, urea, creatinine, blood glucose, international normalized ratio (INR)/prothrombin time (PTT), and complete blood count should be obtained. In addition, specific preoperative investigations need to be reviewed, such as echocardiogram, pulmonary function tests, ECG, and chest radiograph.

There are typically two types of patients presenting for heart transplantation. The first type of patient is relatively compensated, requiring possible IV inotropic support or may even be ambulatory in a nonhospital setting. The second type is moribund and decompensated, requiring mechanical ventilation and/or mechanical circulatory support. At the time of transplant, 44.8% of patients are on IV inotropes, 19% have an LVAD, 6.9% have an IABP, and 2.9% are mechanically ventilated. Only 0.7% require ECMO before transplant. Recipients who have undergone prior cardiac surgery need to be identified, as this will increase the surgical time to achieve CPB due to adhesions and bleeding. Large-bore IV access must be secured and cross-matched blood should be readily available in the operating room before surgery commences. The use of antifibrinolytics is routine for these cases.

Taylor DO, Oz M, Mancini D, et al. Registry of the International Society for Heart and Lung Transplantation: twenty-sixth official adult heart transplant report-2009. *J Heart Lung Transplant*. 2009;28(10):1007–1022.

B.2. How would you premedicate this patient? Why?

Patients should be transported to the operating room with oxygen supplementation. Caution should be exercised with sedative or narcotic premedication. With minimal cardiac reserve, sedation may blunt the patient's respiratory and sympathetic drive and can lead to hypoxemia, hypercapnia, and even hypotension. Antibiotic prophylaxis often is achieved with 1 to 2 g of cephazolin or vancomycin.

Jhaveri R, Tardiff B, Stanley TE III. Anesthesia for heart and heart–lung transplantation. *Anesthesiol Clin N Am*. 1994;12:729–747.

C. Intraoperative Management

C.1. What anesthetic equipment and monitors would you set up? Why?

Anesthetic equipment includes a ventilator with air mixture capability, airway and intubation set-up, fluid/blood warmer, extracorporeal bypass machine with membrane oxygenator, and NO delivery and monitoring system. The patient is taken to the operating room breathing supplemental oxygen. Monitors include a 5-lead ECG, digital pulse oximeter, noninvasive blood pressure cuff, capnography, urinary catheter, temperature probe(s), and peripheral nerve stimulator. All invasive lines are placed with meticulous attention to aseptic technique and titrated sedation. A no.14 g IV line and a no. 20 g radial arterial catheter for continuous blood pressure monitoring are inserted. Routinely, a pulmonary arterial (PA) catheter is inserted via the right internal jugular vein for pre-CPB, post-CPB, and postoperative measurement of PA pressure, PVR, and CO. The PA catheter is withdrawn back to about a 20-cm position in an 80-cm sterile sleeve before cardiectomy. TEE also is very useful in the intraoperative management of the pretransplant and posttransplant periods. A bispectral index monitor may be applied before induction. In some centers, cerebral oximetry also would be used as a monitor of cerebral oxygen delivery.

C.2. What is the role of transesophageal echocardiography (TEE)?

The echocardiographer can provide feedback to the surgeon and anesthesiologist regarding overall function of the transplanted heart. In particular, wall motion abnormalities, end-diastolic volume, and valvular function can be assessed. Of particular interest is RV function and an assessment of PA pressures. TEE also may be useful in the assessment of surgical anastomosis, performed by an echocardiographer with advanced training. Specifically, the main PA anastomosis should be evaluated for stenosis. The long-axis view of the left atrium is composed of recipient and donor tissue and may appear large. If excessive tissue is present, acquired cor triatriatum may develop due to an unfolding of redundant tissue.

Bryan AJ, Barzilai B, Kouchoukos NT. Transesophageal echocardiography and adult cardiac operations. *Ann Thorac Surg.* 1995;59:773–779.

Couture R, Carrier M. Transesophageal echocardiography. In: Denault AY, Couture P, Buithieu J, et al., eds. *A Perioperative Transdisciplinary Approach.* New York: Taylor & Francis Group; 2005:471–480.

Suriani RJ. Transesophageal echocardiography during organ transplantation. *J Cardiothorac Vasc Anesth.* 1998;12:686–694.

C.3. Describe the induction and maintenance of anesthesia.

It is important to time the anesthesia induction and surgery carefully to achieve CPB at the time of donor heart arrival in order to minimize ischemia time, particularly for a re-sternotomy patient. Prompt securing of the airway may be required as the recipient is not always properly fasted for transplantation surgery; however, a rapid induction needs to be balanced against the risk of hemodynamic compromise. The patient is anesthetized with midazolam and fentanyl or sufentanil titrated based on hemodynamic status and level of consciousness. Muscle relaxation may be achieved with pancuronium, rocuronium, cisatracurium, or vecuronium. Succinylcholine usually is not used because of concern of bradycardia during induction, as blood pressure in pre–heart transplant recipients often is heart rate dependent. Maintenance phase is achieved through the use of a balance anesthetic technique. Volatile agents (sevoflurane or isoflurane) are combined with fentanyl or sufentanil, midazolam, and muscle relaxation as required. Nitrous oxide generally is avoided, due to its effect on PVR.

Previously, many centers would have used aprotinin as an antifibrinolytic therapy. However, Bayer, the manufacturer of aprotinin, removed it from the market after concerns of increased mortality surfaced in clinical trials. Tranexamic acid and epsilon-aminocaproic acid have taken this role now in many cardiac transplant centers.

Fergusson DA, Hebert PC, Mazer CD, et al. A comparison of aprotinin and lysine analogues in high-risk cardiac surgery. *NEJM*. 2008;358:2319–2331.

Karkouti K, Beattie SW, Dattilo KM, et al. A propensity score case-control comparison of aprotinin and tranexamic acid in high-transfusion-risk cardiac surgery. *Transfusion*. 2006;46:327–338.

Mangano DT, Tudor IC, Dietzel C. The risk associated with aprotinin in cardiac surgery. *NEJM*. 2006;354:353–365.

C.4. How would you manage this patient during cardiopulmonary bypass (CPB)?

The anesthetic management of CPB in these patients is not different from that in nontransplant patients, except that rewarming usually is prolonged because of the profound cooling of the donor heart and the prolonged ischemic time. Early in the perfusion, mixed venous oxygen desaturation and metabolic acidosis must be corrected. The fluid balance, hematocrit, electrolyte composition, and serum glucose must be monitored closely. During CPB, anesthesia maintenance is achieved by narcotic supplementation, an inhalational agent, and/or benzodiazepine. Once cardiac rhythm has been established and anastomosis of the pulmonary artery is completed, the patient is placed in a head-down position for air evacuation from the left side of the heart. An isoproterenol infusion (1 to 5 μg/min) may be considered to improve contractility and to increase heart rate to about 90 to 110 beats per minute. If necessary, the heart may be externally paced via epicardial leads.

D. Postoperative Management

D.1. What are the early postoperative complications?

The early postoperative complications include:

- Right heart failure/Pulmonary hypertension
- Denervated heart
- Bleeding
- Early graft failure

D.2. What are the mechanisms of early right heart failure?

Right-sided heart failure is an important cause of posttransplant morbidity and mortality. It has a diverse number of causes related to both increases in flow and resistance across the pulmonary vascular bed. One prime cause is long-standing elevation in left ventricular pressure, leading to an increase in pulmonary pressure and vasoconstriction. This pulmonary vasoconstriction may become fixed over time, compromising RV function after transplant. However, a normal preoperative PVR does not rule out the potential for RV failure posttransplant. Poor organ preservation and CPB also can have deleterious effects on graft ventricular function.

Stobierska-Dzierzek B, Awad H, Michler RE. The evolving management of acute right-sided heart failure in cardiac transplant recipients. *J Am Coll Cardiol*. 2001;38:923–931.

D.3. How would you treat right heart failure following heart transplantation?

RV failure is associated with dilation, ischemia, and poor contractility. This can result in a shift of the ventricular septum to the left, with a reduction in left ventricular filling and reduced CO. Basic therapeutic goals are to maintain adequate coronary perfusion, optimize oxygen delivery, prevent further distention of the RV by judicious use of fluids, minimize myocardial oxygen consumption, and reduce PVR to decrease RV afterload.

Phosphodiesterase inhibitors, such as milrinone, which have systemic and pulmonary vasodilatory effects in addition to positive inotropy, are particularly useful. Prostacyclin (PGI_2), prostaglandin E(1), isoproterenol (1 to 5 μg/min), dobutamine, and nitrates also have been used with success to treat RV failure. However, vasodilator use often can be accompanied by arterial hypotension, requiring the administration of vasopressors to maintain adequate coronary perfusion. Inhaled NO also is widely used as a selective pulmonary vasodilator in severe pulmonary hypertension and RV failure. Sildenafil also can be considered when trying to reduce PVR. It should be remembered that simple management goals of avoiding hypoxia, hypercarbia, and excessive positive end-expiratory pressure (PEEP) will help avoid elevated PVR.

In severe cases of refractory RV failure, posttransplant mechanical support should be considered, including IABP, RVAD, or ECMO.

Costanzo MR, Task Force. The International Society of Heart and Lung Transplantation guidelines for the care of heart transplant recipients. *J Heart Lung Transplant.* 2010;29:914–956.

Granton J, Moric J. Pulmonary vasodilators-Treating the right ventricle. *Anesthesiol Clin.* 2008;26:337–353.

Stobierska-Dzierzek B, Awad H, Michler RE. The evolving management of acute right-sided heart failure in cardiac transplant recipients. *J Am Coll Cardiol.* 2001;38:923–931.

D.4. How does inhaled nitric oxide (NO) work as a selective pulmonary vasodilator?

The advantage of inhaled NO as a pulmonary vasodilator lies mainly in the fact that its smooth muscle relaxant effect is limited to the pulmonary vasculature—the half-life in vivo of inhaled NO is only a few seconds. Therefore, it has little effect on the systemic circulation, unlike IV vasodilators, such as nitroprusside, nitroglycerin, prostaglandins, and calcium channel blockers. Furthermore, inhaled NO selectively causes vasodilation in ventilated lung units, thus decreasing $\dot{V}/\dot{Q}$ mismatch and shunt. Inhaled NO (1 to 20 ppm) can result in significant decreases in pulmonary artery pressure, PVR, and central venous pressure (CVP), while increasing mean arterial pressure, CO, and arterial oxygenation. In addition, a TEE documented alteration of the ventricular septal shift with a significant reduction in RV chamber and tricuspid valvular annulus size can be seen.

Girard C, Durand PG, Vedrinne C, et al. Inhaled nitric oxide for right ventricular failure after heart transplantation. *J Cardiothorac Vasc Anesth.* 1993;7:481–485.

Konstadt S. Nitric oxide: has it progressed from molecule of the year to wonder drug of the decade? *J Cardiothorac Vasc Anesth.* 1995;9:625–626.

D.5. What is the pathophysiology of the denervated heart?

Following cardiac transplantation, the cardiac plexus is interrupted and the heart is denervated. The recipient atrium remains innervated but hemodynamically

unimportant, while the donor atrium is denervated and is responsible for the electrophysiologic responses of the transplanted heart. The ECG often contains two P waves. The denervated heart retains its intrinsic control mechanisms, which include the Frank-Starling mechanism and intact alpha- and beta-adrenoreceptor responses to circulating catecholamines. This denervated heart lacks the ability to respond acutely to hypovolemia or hypotension with reflex tachycardia, but responds to stress primarily by an increase in stroke volume. This reflects dependence of the sinus node on direct stimulation by endogenously released catecholamines and the absence of control via neural mechanisms. This is why heart-transplanted patients are said to be "preload dependent." Interestingly, however, some studies have demonstrated reinnervation within a year after transplantation. This has led to symptoms of angina pectoris when ischemia develops in the transplanted heart.

Cheng DCH, Ong DD. Anaesthesia for non-cardiac surgery in heart transplanted patients. *Can J Anaesth*. 1993;40:981–986.

Kobashigawa JA. Postoperative management following heart transplantation. *Transplantation Proceedings*. 1999;31:2038–2046.

D.6. What are the common cardiac dysrhythmias following heart transplant?

A wide variety of arrhythmias can occur in the heart transplant recipient. Early on, the course of recovery from heart transplant bradyarrhythmias is common and often is self-limited. However, this underscores the utility of epicardial pacemaker placement at the time of surgery. The spectrum of other arrhythmias include premature ventricular complexes, atrioventricular (AV) blockade, and supraventricular tachycardia. In fact, 5% to 24% of heart transplant recipients suffer from atrial fibrillation. The causes of arrhythmia include surgical disruption of normal conduction pathways and the sinus node, denervation, rejection, and coronary allograft vasculopathy.

Stecker EC, Sterlich KR, Chugh SS, et al. Arrhythmias after orthotopic heart transplantation. *J Cardiac Failure*. 2005;11(6):464–472.

D.7. What are the causes of posttransplant bleeding?

Perioperative bleeding is a significant cause of mortality following heart transplantation. The causes of posttransplant bleeding are anastomosis leaks and coagulopathy. Immediately before weaning from bypass, with the heart filled, the posterior anastomosis is carefully checked again by the surgeon for "water-tightness," because leaks in this area are more difficult and riskier to repair later. Coagulopathy, or what some term "medical bleeding," often results from a combination of mechanisms, including inadequate heparin reversal, dilution of platelets and coagulation factors, hypothermia, and CPB effects on fibrinolysis, platelet function, and factor activation. In addition, those patients with a ventricular assist device in place before transplant are at particular risk for perioperative hemorrhage.

Bourge RC, Naftel DC, Costanzo-Nordin MR, et al. Pre-transplantation risk factors for death after heart transplantation: a multi-institutional study. *J Heart Lung Transplant*. 1993;12:549–562.

Wegner JA, DiNardo JA, Arabia FA, et al. Blood loss and transfusion requirements in patients implanted with a mechanical circulatory support device undergoing cardiac transplantation. *J Heart Lung Transplant*. 2000;19:504–506.

D.8. How would you treat posttransplant bleeding?

Prevention of potential causes of bleeding is key. The use of antifibrinolytics is strongly encouraged, in particular if re-do sternotomy is to be undertaken. Avoidance of excessive crystalloid in the prebypass period may reduce the dilutional component of coagulopathy. Maintaining normothermia with forced air warming devices and fluid warmers also is imperative. When bleeding is evident in the postoperative period, the judicious use of packed red blood cells, fresh frozen plasma, and platelets is a starting point. If hemorrhage is not responsive to conservative measures, disseminated intravascular coagulopathy must be ruled out. If serum fibrinogen is low (less than 0.8 to 1.0 g/L), then the use of cryoprecipitate should be entertained. Although not routine, desmopressin (0.3 μg/kg) also may have a role in refractory cases. Finally, recombinant factor VIIa has been used successfully to treat hemorrhage in cardiac transplant patients. However, the risk of thrombosis needs to be weighed against the risk of ongoing bleeding, and consultation with a hematologist would be advisable before administration. It always should be remembered that bleeding that is excessive and not clearly secondary to coagulopathy warrants surgical re-exploration.

Costanzo MR, Task Force. The International Society of Heart and Lung Transplantation guidelines for the care of heart transplant recipients. *J Heart Lung Transplant*. 2010;29:914–956.

Kogan A, Berman M, Kassif Y, et al. Use of recombinant factor VII to control bleeding in a patient supported by right ventricular assist device after heart transplantation. *J Heart Lung Transplant*. 2005;24:347–349.

D.9. What are the causes of early graft failure?

Graft failure (primary and nonspecific) is the most common cause of death in the first 30 days after heart transplant. Etiologies include biventricular failure, RV failure (often due to high PVR), flow-limiting coronary stenosis, and hyperacute rejection.

Luckraz H, Goddard M, Charman SC, et al. Early mortality after cardiac transplantation: should we do better? *J Heart Lung Transplant*. 2005;24:401–405.

D.10. How would you manage this patient in the intensive care unit?

Within the first 30 days, posttransplant graft failure (primary and nonspecific), multiorgan failure, and non-CMV infection are the most common causes of death at 41%, 13%, and 13%, respectively. Early management goals include prevention of infection and rejection, treatment of bleeding and dysrhythmias, cardiovascular support, and avoidance of elevated pulmonary artery pressures. If possible, one should aim to wean the patient from the ventilator and extubate within 24 hours. In order to facilitate oxygenation and weaning, strict supervision of fluid balance and body weight is required. Immunosuppression often is achieved with a cocktail of medications, including steroids (methylprednisolone then prednisone); calcineurin inhibitors (tacrolimus, cyclosporine); and antiproliferative agents (mycophenolate mofetil). Leucodepleting agents may be used perioperatively, such as antithymocyte globulin or OKT3. Secondary to immunosuppression, patients often are covered prophylactically with ganciclovir (CMV prophylaxis) and trimethoprim/sulfamethoxazole (*Toxoplasma* and *Pneumocystis carinii* prophylaxis).

Blasco LM, Parameshwar J, Vuylsteke A. Anaesthesia for noncardiac surgery in the heart transplant recipient. *Curr Opin Anaesthesiol*. 2009;22:109–113.

Costanzo MR, Task Force. The International Society of Heart and Lung Transplantation guidelines for the care of heart transplant recipients. *J Heart Lung Transplant*. 2010;29:914–956.

Taylor DO. Cardiac transplantation: drug regimens for the 21st century. *Ann Thorac Surg*. 2003;75:S72–S78.

E. Subsequent Noncardiac Surgery

The patient recovers successfully following heart transplant. However, 2 years postoperatively, he fractures his left radius after a fall. He then presents for open reduction and internal fixation of the fracture.

E.1. How would you monitor this patient?

This patient should have similar monitoring requirements for nontransplant patients undergoing similar procedures. Smooth and safe anesthesia is contingent upon careful preoperative assessment, which may reduce the need for invasive monitoring with all its attendant risks. Adequate preload must be attained preoperatively and intravascular volume status maintained intraoperatively, because these patients are "preload dependent." Monitors in the above case would include an ECG, noninvasive blood pressure cuff, capnometer, oxygen saturation probe, and, if general anesthetic was delivered, a temperature probe, agent-specific gas monitor, and a neuromuscular stimulator would be applied. However, for cases with potential for blood loss and fluid shifts, consideration should be given to additional intraoperative monitors, including an arterial line, central venous line, pulmonary artery catheter, and TEE.

Cheng DCH, Ong DD. Anaesthesia for non-cardiac surgery in heart-transplanted patients. *Can J Anaesth*. 1993;40:981–986.

E.2. What type of anesthetic is best for the heart-transplanted patient?

In a series of 86 heart-transplanted recipients, 18 returned for 32 noncardiac surgical procedures. The breakdown included 18 neurolept-anesthesia cases, 12 general anesthesia cases with a combination of N_2O/O_2/narcotic/relaxant and low doses of volatile agents, and 2 spinal cases. The patients had normal requirements of IV and inhalational agents, muscle relaxants, and local anesthetics. There was no prolonged action of any anesthetic agents. This indicates that the choice of general, neuroleptic, or spinal anesthesia does not affect postoperative outcome in heart-transplanted recipients undergoing subsequent noncardiac surgery.

Blasco LM, Parameshwar J, Vuylsteke A. Anaesthesia for noncardiac surgery in the heart transplant recipient. *Curr Opin Anaesthesiol*. 2009;22:109–113.

Cheng DCH, Ong DD. Anaesthesia for non-cardiac surgery in heart-transplanted patients. *Can J Anaesth*. 1993;40:981–986.

E.3. Which anesthetic technique would you give this patient?

This patient could safely receive general anesthesia or regional blockade of his brachial plexus for the upcoming surgery.

E.4. Do you need to use a muscarinic antagonist with cholinesterase inhibitors to reverse the muscle relaxant in heart-transplanted patients?

Although it does not compromise other hemodynamic parameters, neostigmine has been shown to produce a dose-dependent decrease in heart rate in heart-transplanted patients. In remote transplanted patients (>6 months), a muscarinic antagonist should be administered simultaneously with cholinesterase inhibitors to block the cardiac and muscarinic side effects, as slow development of cardiac reinnervation may be possible.

Ashary N, Kaye AD, Hegazi AR, et al. Anesthetic considerations in the patient with a heart transplant. *Heart Disease.* 2002;4:191–198.

Backman SB, Fox GS, Stein RD, et al. Neostigmine decreases heart rate in heart transplant patients. *Can J Anaesth.* 1996;43:373–378.

Wilson RF, Christensen BV, Olivari MT, et al. Evidence for structural sympathetic reinnervation after orthotopic cardiac transplantation in humans. *Circulation.* 1991;83:1210–1221.

E.5. What are the anesthetic implications for heart-transplanted patients?

The anesthetic implications for heart-transplanted patients include:

- Denervated heart
- Allograft rejection
- Infection due to immunosuppression
- Drug interaction
- Allograft coronary artery disease
- Hypertension
- Renal dysfunction

Ashary N, Kaye AD, Hegazi AR, et al. Anesthetic considerations in the patient with a heart transplant. *Heart Disease.* 2002;4:191–198.

Cheng DCH, Ong DD. Anaesthesia for non-cardiac surgery in heart-transplanted patients. *Can J Anaesth.* 1993;40:981–986.

E.6. What is the significant implication of the denervated heart?

The denervated heart retains its intrinsic control mechanisms, which include Frank-Starling mechanism, impulse formation and conductivity, and responsiveness to circulating catecholamines in the form of increased heart rate and contractility. But the normal respiratory variations or response to carotid sinus massage and Valsalva maneuvers are absent. At rest, the heart rate reflects the intrinsic rate of depolarization at the donor sinoatrial node, and in the absence of any vagal tone, is faster than normal at about 90 to 100 beats per minute. The heart rate shows minimal response to drugs, such as muscle relaxants (pancuronium); anticholinergics (atropine, glycopyrrolate, and scopolamine); cholinesterase inhibitors (neostigmine, edrophonium, pyridostigmine, physostigmine); digoxin, nifedipine, phenylephrine, or nitroprusside, but will respond to isoproterenol, ephedrine, dopamine, and epinephrine.

Cardiac dysrhythmias may occur in heart-transplanted patients. First-degree AV block is common. Dual AV nodal pathways frequently are observed, but re-entry dysrhythmias are rare. Bradyarrhythmic therapy in these patients should be treated with a direct beta-adrenergic stimulating agent (epinephrine, isoproterenol). Medications used to treat tachyarrhythmias (calcium channel blockers, beta-blockers) need to be used with caution due to their negative inotropic effects.

Ashary N, Kaye AD, Hegazi AR, et al. Anesthetic considerations in the patient with a heart transplant. *Heart Disease*. 2002;4:191–198.

Blasco LM, Parameshwar J, Vuylsteke A. Anaesthesia for noncardiac surgery in the heart transplant recipient. *Curr Opin Anaesthesiol*. 2009;22:109–113.

Stein KL, Darby JM, Grenvik A. Intensive care of the cardiac transplant recipient. *J Cardiothorac Anesth*. 1988;2:543–553.

E.7. What is the significance of allograft rejection?

The majority of rejection episodes occur in the first 6 months posttransplant. These patients can present with fever, malaise, arrhythmias, and shortness of breath. Hemodynamic compromise is considered a late sign of rejection. The gold standard for diagnosis is endomyocardial biopsy. Rejection episodes are treated primarily with steroids; however, more severe forms may require more aggressive immunosuppression with IV immunoglobulin or plasmapheresis.

Costanzo MR, Task Force. The International Society of Heart and Lung Transplantation guidelines for the care of heart transplant recipients. *J Heart Lung Transplant*. 2010;29:914–956.

Kobashigawa JA. Postoperative management following heart transplantation. *Transplantation Proceedings*. 1999;31:2038–2046.

E.8. What is the significance of infection in these patients?

Immunosuppressive drugs are continued indefinitely in heart-transplanted patients and infection remains a major cause of death, with 10% of mortality 5 years posttransplant secondary to non-cytomegalovirus (CMV) infections. Early postoperative bacterial infections (e.g., mediastinitis) and opportunistic infections (e.g., CMV, *P. carinii*, *Toxoplasma*) are of great concern. Invasive monitoring techniques and all forms of instrumentation should be kept to the minimum consistent with safe anesthesia. Attention to sterile technique should be paramount. Intubation via the orotracheal route is preferable to the nasotracheal route as the latter is associated with infection by diphtheroids and staphylococcal organisms from the nasopharynx and skin.

Blasco LM, Parameshwar J, Vuylsteke A. Anaesthesia for noncardiac surgery in the heart transplant recipient. *Curr Opin Anaesthesiol*. 2009;22:109–113.

Shaw IH, Kirk AJB, Conacher ID. Anaesthesia for patients with transplanted hearts and lungs undergoing non-cardiac surgery. *Br J Anaesth*. 1991;67:772–778.

Taylor DO, Oz M, Mancini D, et al. Registry of the International Society for Heart and Lung Transplantation: twenty-sixth official adult heart transplant report-2009. *J Heart Lung Transplant*. 2009;28(10):1007–1022.

E.9. What are the significant implications of drug interactions?

Chronic steroid treatment may result in an abnormal stress response, so patients should receive perioperative steroid coverage. Azathioprine has been reported to antagonize the competitive neuromuscular-blocking drugs by its phosphodiesterase-inhibiting properties, therefore larger doses of relaxants may be required. In experimental animals, cyclosporine infusions have been shown to potentiate the neuromuscular-blocking effects of atracurium and vecuronium, and single doses of cyclosporine may result in increased duration of action of both barbiturates and narcotics.

Ashary N, Kaye AD, Hegazi AR, et al. Anesthetic considerations in the patient with a heart transplant. *Heart Disease*. 2002;4:191–198.

Cirella VN, Pantuck CB, Lee YJ, et al. Effects of cyclosporine on anesthetic action. *Anesth Analg*. 1987;66:703–706.

E.10. What is cardiac allograft vasculopathy (CAV)? Why is this important?

The transplanted heart is vulnerable to an accelerated process of coronary atherosclerosis called cardiac allograft vasculopathy (CAV). Between the 1st and 10th year posttransplant, 44% of patients develop CAV. It is characterized by concentric intimal proliferation and diffuse narrowing along the coronary vessel. Diagnosis is accomplished by coronary angiography or intravascular ultrasound. The etiology is likely multifactorial, with both immunologic and nonimmunologic factors. Risk factors for CAV development within 8 years posttransplant include donor hypertension, induction therapy with IL-2 antagonists or OKT3, pretransplant coronary disease, clinical infection in donor, older donor age, and decreasing recipient age.

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E.11. What is the significant implication of posttransplant hypertension?

After 10 years, 97% of surviving patients have developed hypertension. Cyclosporine often is cited as a causative factor. Current therapy may consist of a calcium channel blocker such as diltiazem. However, care must be taken, as diltiazem may increase cyclosporine serum levels. Nifedipine has a tendency to cause significant vasodilatation and may be tolerated poorly in these patients. When necessary, an ACE inhibitor may be added. Because cardiac responsiveness during exercise is dependent on circulating catecholamines, beta-blockers often are avoided after heart transplantation.

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E.12. What is the significant implication of renal dysfunction?

Renal dysfunction is found in 31% of recipients at 5 years. Due to the nephrotoxic effects of cyclosporine, serum creatinine concentrations gradually increase after

cardiac transplantation, but generally plateau around 170 to 180 mmol/L^{-1}. Anesthetic drugs that are excreted mainly by renal clearance should be avoided if renal function is compromised. Also, one needs to be mindful of medications that may compromise further renal function, such as nonsteroidal anti-inflammatory drugs (NSAIDs).

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E.13. Is ambulatory surgery appropriate for heart transplant recipients?

Unfortunately, there is a paucity of evidence supporting either the safety or harm of ambulatory surgery in heart transplant recipients. In addition, the choice of anesthetic technique seems to have no influence on outcome. Regardless, these patients should be seen in preadmission clinics before the day of surgery and have appropriate screening tests done preoperatively, including, but not limited to, an assessment of complete blood count, electrolytes, renal function, ECG, and an accurate blood pressure measurement. They also should be evaluated by the cardiology transplant service and if any concern is raised, further testing should be undertaken, such as echocardiography, coronary angiography, or endomyocardial biopsy. Recommendations also should be obtained from the cardiac transplant service regarding perioperative antibiotic prophylaxis and immunosuppression.

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CHAPTER 13

Ischemic Heart Disease and Noncardiac Surgery

SHAMSUDDIN AKHTAR, MARBELIA GONZALEZ, J. PATRICIO ESCANDON, AND PAUL G. BARASH

A 72-YEAR-OLD MAN

is scheduled for right hemicolectomy for colon cancer. Past history reveals a myocardial infarction (MI) 5 months ago and placement of a right coronary artery stent. He also has diabetes mellitus type 2. He is treated with atenolol, diltiazem, glyburide, losartan, and an occasional sublingual nitroglycerin (NTG).

A. Medical Disease and Differential Diagnosis

1. What are the preoperative predictors for major adverse cardiac events (MACE) perioperatively?
2. What are the determinants of myocardial oxygen demand? How are they measured clinically?
3. What factors determine myocardial oxygen supply?
4. What is the mechanism of perioperative myocardial ischemia and infarction?
5. What is the incidence of perioperative reinfarction for noncardiac surgery?
6. Based on his history of MI, would you recommend that the surgery be postponed for a certain period of time? If so, why?
7. State the perioperative medical therapy you would employ to reduce the incidence of myocardial ischemia.
8. Would the patient have increased risk for perioperative major cardiac complications if the patient's preoperative electrocardiogram (ECG) shows right bundle branch block (RBBB)/left bundle branch block (LBBB)?
9. Would you recommend that this elective colectomy be postponed, if the patient underwent placement of a coronary artery bare metal stent 3 weeks ago or a drug-eluting stent (DES) and is taking aspirin and clopidogrel (Plavix)?

B. Preoperative Evaluation and Preparation

1. How would you evaluate the patient's cardiac condition? What laboratory tests would you like to order?
2. Would you recommend further cardiac testing or coronary revascularization before surgery?

3. How would you classify the cardiac risk according to the type of surgery?
4. Are patients with a Q-wave infarction at greater risk for perioperative reinfarction than those with a non–Q-wave infarction?
5. What is the role of exercise or pharmacologic stress test for this patient?
6. Would you discontinue any medication before surgery?
7. How would you premedicate this patient?
8. Is there a role for α_2-agonists in premedication?

C. Intraoperative Management

1. What are the intraoperative predictors for perioperative cardiac morbidity (PCM)?
2. How would you monitor the patient in the operating room?
3. What ECG leads would you monitor? Why V_5?
4. Would you use a pulmonary artery catheter (PAC)?
5. Would you use transesophageal echocardiography (TEE) as a monitor?
6. Is regional anesthesia better than general anesthesia for patients with cardiac disease?
7. How would you induce general anesthesia?
8. Would you induce anesthesia with etomidate? Why?
9. What is the best choice of anesthetic agents for maintenance of anesthesia? Why?
10. What muscle relaxant would you choose? Why?
11. You notice a new 3-mm ST-segment depression in lead V_5. How would you treat it?
12. Would you give prophylactic intravenous NTG to prevent myocardial ischemia?
13. What is the significance of tight control of the heart rate intraoperatively?
14. When would you extubate the trachea in this patient? What could you do to prevent hypertension and tachycardia during extubation and emergence?

D. Postoperative Management

1. What are the postoperative predictors of PCM?
2. How would you control postoperative pain?
3. Is postoperative anemia associated with adverse cardiac outcome?
4. Is postoperative hypothermia associated with postoperative myocardial ischemia?
5. How would you make a diagnosis of perioperative myocardial infarction (PMI)?
6. How would you manage the patient with a suspected PMI?

A. Medical Disease and Differential Diagnosis

A.1. What are the preoperative predictors for major adverse cardiac events (MACE) perioperatively?

PMI is one of the most important predictors of short- and long-term mortality and morbidity associated with noncardiac surgery. Therefore, the prevention of PMI relates to improvement in postoperative outcomes. Numerous risk indices and predictors for perioperative cardiac morbidity (PCM) have been published over the last 30 years.

In 1999, Lee et al. revised the Goldman Cardiac Risk Index, utilizing six independent predictors of cardiac risk:

- High-risk type of surgery
- History of ischemic heart disease (IHD)
- History of congestive heart failure (CHF)
- History of cerebrovascular disease
- Preoperative treatment of diabetes mellitus with insulin
- Preoperative serum creatinine greater than 2.0 mg per dL

They concluded that the rate of major cardiac complications (MI, pulmonary edema, ventricular fibrillation, and primary cardiac arrest) with 0, 1, 2, and more than or equal to 3 predictors, were 0.5%, 1.3%, 4%, and 9%, respectively.

According to the 2009 American College of Cardiology (ACC) and American Heart Association (AHA) guideline update on perioperative cardiovascular evaluation (ACC/AHA guidelines), clinical predictors of MACE are categorized into major, intermediate, and minor factors as follows:

Major predictors

- Unstable coronary syndromes
  - Acute (MI ≤7 days before examination) or recent MI (>7 days but ≤1 month) with evidence of important ischemic risk by clinical symptoms or noninvasive study. Notice that the traditional 3 and 6 months interval had been avoided.
- Unstable or severe angina (Canadian class III: marked limitation of ordinary physical activity; walking one to two blocks on the level and climbing one flight of stairs in normal conditions at normal pace; and Canadian class IV: inability to carry on any physical activity without discomfort—anginal syndrome may be present at rest.)
- Decompensated heart failure
- Significant arrhythmias
  - High-grade atrioventricular block, Mobitz type II atrioventricular block, third degree heart block
  - Symptomatic ventricular arrhythmias
  - Supraventricular arrhythmias (including atrial fibrillation) with uncontrolled ventricular rate (heart rate greater than 100 beats per minute at rest)
  - Symptomatic bradycardia
- Severe valvular disease (severe aortic stenosis valve area <1 cm^2 or symptomatic) or symptomatic mitral stenosis

Intermediate predictors

- History of IHD, including stable angina pectoris (Canadian class I: ordinary physical activity, such as walking and climbing stairs, does not cause angina; angina is with strenuous or rapid or prolonged exertion at work or recreation. Canadian class II: slight limitations to ordinary activity. Walking or climbing stairs rapidly; walking uphill; walking or stair climbing after meals, or in cold, or in wind, or under emotional stress, or only during the few hours after awakening. Walking more than two blocks on the level and climbing more than one flight of ordinary stairs at a normal pace and in normal conditions.)
- History of compensated or prior heart failure
- History of cerebrovascular disease
- Diabetes mellitus
- Renal insufficiency

Minor predictors

- Advanced age (>70 years)
- Abnormal ECG (left ventricular [LV] hypertrophy, LBBB, ST-T abnormalities)
- Rhythm other than sinus (e.g., atrial fibrillation)

- Low functional capacity (e.g., inability to climb one flight of stairs while carrying a bag of groceries)
- Uncontrolled systemic hypertension

Fleisher LA, Beckman JA, Brown KA, et al. 2009 ACCF/AHA focused update on perioperative beta blockade incorporated into the ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation.* 2009;120:e169–e276.

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A.2. What are the determinants of myocardial oxygen demand? How are they measured clinically?

The three major determinants of myocardial oxygen demand are (1) myocardial LV wall tension (LV preload and afterload), (2) cardiac contractility, and (3) heart rate.

A.3. What factors determine myocardial oxygen supply?

The factors determining myocardial oxygen supply include cardiac output, arterial oxygen content, heart rate, aortic diastolic pressure, LV end-diastolic pressure, patency of coronary arteries, and coronary vascular tone.

A.4. What is the mechanism of perioperative myocardial ischemia and infarction?

Myocardial ischemia occurs whenever myocardial oxygen supply does not match myocardial oxygen demand. Intraoperative ischemia can be precipitated by increases in myocardial oxygen demand caused by tachycardia, hypertension, anemia, stress, sympathomimetic drugs, or discontinuation of β-blockers. However, as many as 50% or more of the ischemic episodes may be unrelated to the indices of oxygen demand, suggesting decreased oxygen supply as the primary cause. Potential etiologies for decreased supply include external factors, such as hypotension, tachycardia, increased filling pressures, anemia, hypoxemia, and decreased cardiac output. In addition, internal factors such as acute coronary artery thrombosis and spasm also may play a role, although no data are available for determining their importance in the perioperative setting.

PMI is one of the most important predictors of short- and long-term morbidity and mortality associated with noncardiac surgery. Unfortunately, the exact nature of PMI remains uncertain and a subject of debate and controversy. The interaction between morphologic and functional factors is unpredictable. There is some pathologic and angiographic evidence that the etiology of PMI resembles that in the nonsurgical setting. In PMI, acute plaque disruption and hemorrhage in the infarct-related coronary artery seems to be common, but the severity of underlying coronary artery stenosis does not necessarily predict the infarct territory. The high incidence of histologically confirmed transmural infarctions seems to be contradictory to the ECG finding of almost exclusively non–Q-wave PMIs. On the other hand, the presence of subendocardial PMIs is consistent with a myocardial oxygen supply/demand mismatch

being the main trigger of myocardial injury. However, myocardial oxygen supply/demand mismatch and plaque rupture are not mutually exclusive mechanisms, and MIs may develop by different mechanisms at different locations in the same patient.

Most PMIs (>80%) occur early after surgery (0 to 72 hours), are asymptomatic, of the non– Q-wave type (60% to 100%), and are commonly preceded by ST-segment depression rather than ST-segment elevation. Long duration (single duration >20 to 30 minutes or cumulative duration >1 to 2 hours intraoperatively or postoperatively) rather than just the presence of postoperative ST-segment depression, seems to be the important factor associated with adverse cardiac outcome.

Landesberg's review of PMIs summarizes pathophysiology as follows:

- Ischemia occurs (67%) at the end of anesthesia or immediately after surgery, during a period characterized by high sympathetic output, hypercoagulability, hypertension, and tachycardia. Ischemia in this period is usually silent, with only ST-segment depression as a marker. And in at least one-third of the patients, this ST depression goes unnoticed.
- Patients with prolonged ST depression may present with troponin elevation, half of them asymptomatic. In this population, the diagnosis of PMI will be missed if troponins were not requested. The elevation may start within the first 8 hours postsurgery.
- Because the increase in troponin occurs during or shortly after prolonged ST-depression–type ischemia, without sudden conversion to ST elevation, it is assumed that PMI is most likely the consequence of stress-induced ischemia and not because of plaque rupture, however, the two mechanisms are not mutually exclusive.
- In approximately 50% of the patients who die secondary due to a PMI, no plaque rupture or thrombosis was found in their coronary arteries at autopsy, despite their extensive coronary artery disease (CAD). The peak incidence of cardiac death in these patients is within the first 3 postoperative days, corresponding to the peak incidence of prolonged, stress-induced, ST-depression–type PMI. The other 50% of patients with PMI, in whom plaque rupture or coronary thrombosis is detected, the timing of death is evenly distributed in the postoperative period, with no special correlation to the end of surgery (Fig. 13.1).

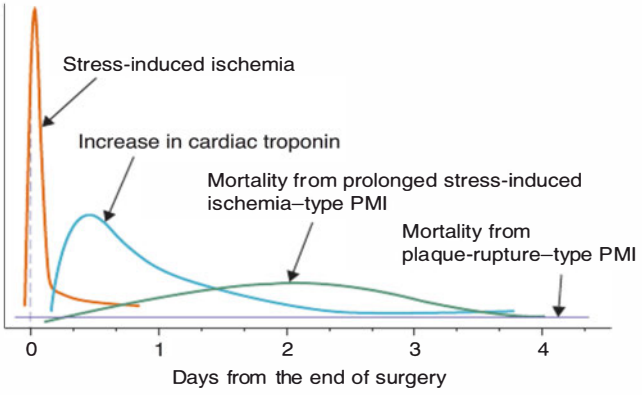

Figure 13.1 The time sequence of perioperative ischemia, infarction, and cardiac death after noncardiac surgery. PMI, perioperative myocardial infarction. (Reprinted with permission from Landesberg G. Pathophysiology of perioperative myocardial infarction: facts and perspectives. *J Cardiothorac Vasc Anesth.* 2003;17:90–100.)

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A.5. What is the incidence of perioperative reinfarction for noncardiac surgery?

Previously, risk assessment for noncardiac surgery of patients with CAD was based upon the time interval between the MI and surgery. However, with improvements in perioperative care, this difference has become blurred. The importance of the timing of the MI in relation to the proposed surgical procedure may no longer be valid in the era of thrombolytics, angioplasty, and risk stratification. Although many patients with a history of an MI may continue to have myocardium at risk, others may not. If a stress test does not indicate residual myocardium at risk, the likelihood of reinfarction is low. There is no data available to quote a perioperative reinfarction rate related to the age of the MI; despite this, statements contained in the current AHA/ACC guidelines for perioperative cardiovascular evaluation confers a higher risk if the MI is at least 1 month old.

Landesberg states that early mortality after PMI ranges from 3.5% to 25% and is higher among patients with marked troponin elevation compared with patients with minor troponin elevation (0% to 7%). This is in contrast to older data that reported a very high incidence of mortality.

Fleisher LA, Beckman JA, Brown KA, et al. 2009 ACCF/AHA focused update on perioperative beta blockade incorporated into the ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for non-cardiac surgery: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2009;120:e169–e276.

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Slogoff S, Keats A. Myocardial ischemia revisited. *Anesthesiology*. 2006;105:214–216.

A.6. Based on his MI, would you recommend that the surgery be postponed for a certain period of time? If so, why?

The arbitrary delaying of a surgical procedure is not supported by the ACC/AHA guidelines. According to these guidelines, an acute MI (≤7 days before the preoperative evaluation) or recent MI (>7 days but ≤1 month) with evidence of important ischemic risk by clinical symptoms or noninvasive study is a major predictor of PCM. Therefore, the separation of the interval of MI to operation into the traditional 3- and 6-month intervals is no longer recommended. Current management of MI provides for risk stratification during convalescence period. If a recent stress test does not indicate residual myocardium at risk, the likelihood of reinfarction after noncardiac

surgery is low. Although there are no adequate clinical trials on which to base firm recommendations, it appears reasonable to wait 4 to 6 weeks after MI to perform elective surgery due to the decrease in incidence of fatal arrhythmias and ventricular rupture after this period of time.

Fleisher LA, Beckman JA, Brown KA, et al. 2009 ACCF/AHA focused update on perioperative beta blockade incorporated into the ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation.* 2009;120:e169–e276.

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A.7. State the perioperative medical therapy you would employ to reduce the incidence of myocardial ischemia.

β-Adrenergic antagonists (esmolol, atenolol, metoprolol, bisoprolol)

This drug class:

- Reduces myocardial oxygen consumption
- Improves coronary blood flow
  - Prolonged diastolic perfusion period
  - Improved collateral flow
  - Increased flow to ischemic areas
- Improves supply/demand ratio
- Stabilizes cellular membranes
- Improves oxygen dissociation from hemoglobin (Hgb)
- Inhibits platelet aggregation

β-Blockers suppress perioperative tachycardia and appear most efficacious in preventing perioperative myocardial ischemia. They are well tolerated by most surgical patients and may reduce long-term cardiac events.

Since the 1980s, evidence suggests tachycardia as a major determinant of perioperative ischemia and its relation with the occurrence of MI in the postoperative period.

Slogoff et al. found that PMI presented more frequently in patients that sustained ischemia independent of the time of occurrence. Ischemia was significantly related to tachycardia but not hypertension or hypotension and was frequently seen in the absence of any hemodynamic abnormalities. Also, they advocated the perioperative use of β-blockers to prevent ischemia.

Mangano et al. reported a beneficial effect of atenolol in a randomized double-blind, placebo-controlled trial on overall survival and cardiovascular morbidity in noncardiac surgery patients with or at risk for CAD. Poldermans et al. reported that the β-blocker, bisoprolol, reduced the perioperative incidence of death from cardiac causes and nonfatal MI in vascular surgical patients with known CAD. Bisoprolol, started before noncardiac surgery (30 days), can substantially reduce perioperative cardiac complications in all but the highest-risk patients. However, results of recent trials have not shown efficacy of high-dose, acutely administered, perioperative β-blockers to reduce overall mortality in patients undergoing noncardiac surgery. The largest of these trials, the POISE study, did show better perioperative *cardiac* outcomes with β-blocker use, however, *increased mortality* and stroke rate also was noted in the β-blocker group. Interestingly, the sub-analysis of vascular surgery patients

in the study, demonstrated efficacy of perioperative β-blockers. Currently, the only class I recommendation for perioperative β-blockers use by the AHA is to continue their use in the patients who are already on β-blockers. Patients undergoing vascular surgery who have multiple risk factors or have reversible ischemia on preoperative testing may benefit from perioperative β-blockers (class IIa). Although there are some differences between the European Society of Cardiology (ESC) and the AHA guidelines, they both agree that if β-blockers are used for prophylactic purposes, they should be slowly titrated (at least a week prior to elective surgery) and acute administration of high-dose β-blockers in high-risk population is not recommended.

α_2-Adrenergic agonist (clonidine)

The ACC/AHA guidelines mention the potential benefits on PMI reduction with the use of this drug class (class IIb recommendation). Their benefits had been reviewed by two meta-analysis and two randomized trials. The meta-analysis has shown the reduction of MI/ischemia in vascular patients, but not in all patient groups. A recent randomized trial suggests that using perioperative transdermal/oral clonidine reduced perioperative ischemia and mortality by 31%. There are no prospective trials comparing the two forms of adrenergic modulators (β-blockers vs. α_2 agonists).

Nitrovasodilators (nitroglycerin, isosorbide dinitrate)

Nitrates are associated with the following:

- Decreased LV preload (low dose)
  - Systemic venous dilation
  - Pulmonary arterial bed dilation
  - Pulmonary vein dilation
  - Decreased LV filling pressure
  - Decrease in LV diastolic compressive forces
  - Decreased LV diastolic chamber size
- Decreased LV afterload (high dose)
  - Decreased systolic pressure
  - Decreased systemic vascular resistance
  - Decreased aortic impedance
- Coronary circulation
  - Coronary artery and arteriolar dilation (high dose)
  - Spasm reversal or prevention
  - Stenosis dilation
  - Increased collateral flow
  - Improvement of regional subendocardial ischemia

NTG, one of the oldest antianginal therapies, has had very few trials in noncardiac surgery to evaluate its role in perioperative ischemia reduction. One meta-analysis suggests that nitrates do not reduce perioperative cardiac events. However, a recent meta-analysis published in the Cochrane database has suggested that nitrates show an improvement in perioperative ischemia over placebo. Auerbach and Goldman recommend continuing antianginal medications during the perioperative period. However, the use of prophylactic intravenous NTG is not recommended.

Calcium channel blockers (verapamil, diltiazem, nifedipine, nicardipine)

Calcium channel blockers reduce myocardial oxygen demand by depression of myocardial contractility and dilation of coronary and collateral vessels, which improves blood flow. However, its most important effects may be the prevention of sympathetically mediated coronary vasoconstriction.

Calcium channel blockers interact with the L-type calcium channel and are composed of drugs from five classes: (1) the 1,4-dihydropyridine (DHP) derivatives, rep-

resented by nifedipine, nicardipine, nimodipine, clevidipine and nitrendipine; (2) the phenylalkylamines, represented by verapamil; (3) the benzodiazepines, represented by diltiazem; (4) the diarylaminopropylamine ester, represented by bepridil; and (5) diphenylpiperazine.

Due to the initial experience with nifedipine, increase incidence of MI, there has been reluctance to use this drug class. A meta-analysis of perioperative calcium channel blockers in noncardiac surgery (11 studies involving 1,007 patients) showed significantly reduced ischemia and postoperative supraventricular tachycardia. The beneficial effects were mostly due to the use of diltiazem, and the use of DHP was associated with ischemia. Another study in 1,000 patients having acute or elective aortic aneurysm surgery showed that DHP calcium channel blocker use was independently associated with an increased incidence of perioperative mortality. The use of short-acting DHP, in particular nifedipine capsules, should be avoided. Though the AHA makes no specific recommendations for the prophylactic use of calcium channels blockers, ESC recommends their continued use in patients with Prinzmetal angina pectoris (class I) and for heart rate control in patients with who have contraindications to β-blocker use (class IIb). Routine use of calcium channel blockers to reduce the risk of perioperative cardiovascular complications is not recommended (class III).

Aspirin

Aspirin (acetylsalicylic acid) inhibits platelet aggregation by blocking the production of thromboxane A_2 through a covalent acetylation of a serine residue near the active site of cyclooxygenase. This enzyme produces the cyclic endoperoxide precursor of thromboxane A_2. Acute withdrawal of aspirin may increase the risk of acute coronary syndrome at 8 to 10 days after discontinuation. However, if continued during the perioperative period, aspirin may increase the risk of bleeding. A large meta-analysis, including 41 studies in 49,590 patients, which compared perioprocedural withdrawal versus bleeding risks of aspirin, concluded that the risk of bleeding complications was increased by 1.5 but that aspirin did not lead to higher severity levels of bleeding complications. A systematic review in subjects at risk for, or with IHD, demonstrated that aspirin non-adherence/withdrawal was associated with a threefold higher risk of MACE. Aspirin should only be discontinued if the bleeding risk outweighs the potential cardiac benefit.

Statins

Statins are primarily used for their lipid lowering effects and are widely prescribed in patients with or at risk for IHD. Statins also induce coronary plaque stabilization by decreasing lipid oxidation, inflammation, matrix metalloproteinase, and cell death. These so-called non-lipid or pleiotropic effects may prevent plaque rupture and subsequent MI in the perioperative period. Many trials and observational studies have demonstrated a beneficial effect of perioperative statin use. A meta-analysis of 223,010 patients from 12 retrospective and three prospective trials showed that statins reduced mortality significantly by 44% in noncardiac surgery and by 59% in vascular surgery. The most recent randomized controlled trial was the DECREASE III study. A total of 497 vascular surgery patients were allocated to either fluvastatin (extended release 80 mg once daily) or placebo, starting 37 days prior to surgery. The incidence of myocardial ischemia and cardiac death was almost decreased by 50% in patients allocated to fluvastatin. Both the AHA and ESC guidelines recommend continuing statin therapy for patients currently taking statins and scheduled for noncardiac surgery (class I). ESC also recommends that statins be started in high-risk surgery patients, optimally between 30 days and at least 1 week before surgery (class I B).

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A.8. Would the patient have increased risk for perioperative major cardiac complications if the patient's preoperative electrocardiogram (ECG) shows right bundle branch block (RBBB)/left bundle branch block (LBBB)?

A retrospective, cohort-controlled study of all noncardiac, nonophthalmologic, adult patients showed that the presence of RBBB or LBBB was not associated with a higher incidence of postoperative cardiac complications. Nevertheless, the patients with LBBB may not tolerate certain stress of perioperative noncardiac complications, such as severe sepsis. The presence of LBBB or RBBB may alert the clinician to the possibility of occult CAD or impaired LV function.

Alternatively, in men, but not in women, LBBB was associated with a significantly greater prevalence of cardiac enlargement and CHF than RBBB. The Framingham Study concluded that in an ambulatory population, men with LBBB were more likely to have or subsequently develop advanced cardiovascular abnormalities than were men with RBBB. In women, however, the clinical scenarios that correlate with the two conduction abnormalities are similar.

The ACC/AHA recommends careful evaluation for underlying cardiopulmonary disease, drug toxicity, or metabolic abnormality. Frequent premature ventricular complexes or nonsustained ventricular tachycardia have not been associated with increased risk of MI or cardiac death.

Dorman T, Breslow M, Pronovost PJ, et al. Bundle-branch block as a risk factor in noncardiac surgery. *Arch Intern Med*. 2000;160:1149–1152.

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A.9. Would you recommend that this elective colectomy be postponed, if the patient underwent placement of a coronary artery bare metal stent 3 weeks ago or a drug-eluting stent (DES) and is taking aspirin and clopidogrel (Plavix)?

Extremely high mortality rates (up to 20%) have been reported secondary to acute stent thrombosis, if surgery is performed within weeks after coronary stenting, with discontinuation of antiplatelet therapy. When surgery was performed within this period, discontinuation of dual antiplatelet therapy was associated with an increased incidence of stent thrombosis. After 3 months, patients can be sent for noncardiac surgery, with continuation of at least aspirin therapy.

Current recommendations for the antiplatelet therapy after percutaneous coronary intervention (PCI) with stenting (bare metal stents) is that patients should take aspirin and other platelet inhibitor (ticlopidine, clopidogrel) for at least a full 30 to 45 days to prevent restenosis and allow reendothelialization of the stent to be completed. Therefore, it is prudent to postpone the elective surgery for a minimum of 30 to 45 days (minimum of 6 weeks by ESC recommendations). Also see Chapter 9, section A.5, Figure 9.1.

Though DES delay in-stent thrombosis, their major drawback is the need for prolonged dual antiplatelet therapy by aspirin and clopidogrel for at least 12 months. Retrospective and case series have shown that when surgery was performed within this period, discontinuation of dual antiplatelet therapy was associated with an increased incidence of stent thrombosis. It is now recommended that after DES implantation, elective surgery should not take place until after at least 12 months of continuous dual antiplatelet therapy. Even after 12 months, patients should be sent for noncardiac surgery, with continuation of at least aspirin therapy. The need and timing for surgery should be based on the specific pathology (e.g. malignant tumor, vascular aneurysm repair) and should be balanced against the excessive risk of stent thrombosis and fatal perioperative event during the first year following DES implantation. A careful "case-by-case" consideration is advisable. Discussion between the anesthesiologist, the surgeon, and the treating cardiologist is recommended. Also see Chapter 9, section A.5, Figure 9.2.

The role of preoperative coronary revascularization has been controversial for many years. Few randomized clinical trials and many small size studies have reported conflicting results. Some literature supports revascularization arguing that high-risk cardiac patients who have had PCI performed up to 18 months preoperatively have a lower incidence of perioperative MACE following vascular surgery. However, McFalls et al. published a randomized study where they concluded that coronary revascularization before vascular surgery does not significantly alter the long-term cardiovascular outcome in patients with stable cardiac symptoms. A recent meta-analysis and subsequent publication of the second prospective randomized trial, the Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echo–V (DECREASE-V) pilot study, all failed to show survival benefit associated with preoperative revascularization.

The AHA and ESC guidelines state that the indications for coronary artery bypass grafting (CABG) and PCI should be the same as in the nonsurgical settings. These interventions are rarely indicated to "get a patient through" noncardiac surgery.

Abualsaud AO, Eisenberg MJ. Perioperative management of patients with drug-eluting stents. *J Am Coll Cardiol Intv.* 2010;3:131–142.

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Howard-Alpe GM, de Bono J, Hudsmith L, et al. Coronary artery stents and non-cardiac surgery. *Br J Anaesth.* 2007;98:560–574.

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B. Preoperative Evaluation and Preparation

B.1. How would you evaluate the patient's cardiac condition? What laboratory tests would you like to order?

The initial history, physical examination, and electrocardiographic assessment should focus on identification of potentially serious cardiac disorders, including CAD (e.g., prior MI, angina pectoris), CHF, and electrical instability (e.g., symptomatic arrhythmias).

In addition to identifying the presence of pre-existing manifested heart disease, it is essential to define disease severity, stability, and prior treatment. Other factors that help determine cardiac risk include functional capacity, age, comorbid conditions (e.g., diabetes mellitus, peripheral vascular disease, renal dysfunction, chronic pulmonary disease), and type of surgery (vascular procedures and prolonged, complicated thoracic, abdominal, and head and neck procedures are considered higher risk).

This patient is an insulin-dependent diabetic. Diabetes is associated with a twofold to fourfold increase in the risk of developing CAD. The risk of a MI in patients with diabetes and no evidence of CAD match that of patients without diabetes who have had a previous MI. In patients with CAD and diabetes, the mortality rate can be up to 70% in 10 years. In addition, patients will have a worse outcome for any CAD manifestation.

The preoperative workup varies according to the presence or absence of clinical indicators of underlying CAD:

- Exercise tolerance—poor exercise tolerance has been associated by some with twofold higher odds for postoperative complications. Lee, however, did not find an independent association of functional status with increased risk.
- Evaluation of the presence or absence of any coronary syndrome/symptoms after coronary revascularization.
- Determination of stress test results post-MI/revascularization and establishment of new symptoms since coronary revascularization.

For this patient, the preoperative laboratory workup should include a Hgb/hematocrit (Hct), prothrombin time, partial thromboplastin time, electrolytes, creatinine, and blood urea nitrogen.

Di Carli M, Hachamovitch R. Should we screen for occult coronary artery disease among asymptomatic patients with diabetes? *J Am Coll Cardiol.* 2005;45:50–53.

Fleisher LA, Beckman JA, Brown KA, et al. 2009 ACCF/AHA focused update on perioperative beta blockade incorporated into the ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation.* 2009;120:e169–e276.

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B.2. Would you recommend further cardiac testing or coronary revascularization before surgery?

Successful perioperative evaluation and treatment of cardiac patients undergoing noncardiac surgery requires careful teamwork and communication between patient, primary care physician, anesthesiologist, and surgeon. In general, indications for further cardiac testing and treatment are the same as those in the nonoperative setting, but their timing is dependent on factors such as the urgency of noncardiac surgery, the patient's risk factors, and specific surgical considerations. Preoperative testing should be limited to circumstances in which the results will affect patient treatment and outcomes. A conservative approach to the use of expensive tests and treatments is recommended. Coronary revascularization before noncardiac surgery to enable the patient to "get through" the noncardiac procedure is inappropriate. However, in a high-risk subset of patients, left main disease, severe multivessel disease, severe aortic stenosis, and ejection fraction of less than 20% revascularization/valve replacement may be indicated. Currently, there is overwhelming agreement that aggressive medical management to provide myocardial protection during the perioperative period is a very important element in the reduction of perioperative cardiovascular complications.

Several studies have suggested that a stepwise approach to the assessment of CAD is both efficacious and cost effective. The patient sustained a MI 5 months ago managed with a bare metal stent and was scheduled for an intermediate-risk procedure, hemicolectomy. If the patient has more than 4 METs of physical activity, without chest pain or shortness of breath, if no new cardiac symptoms are present since the revascularization, and the resting ECG showed no new changes compared to 5 months ago, the patient can undergo anesthesia and surgery without further testing. If any of these factors are positive, then exercise thallium imaging or dipyridamole-thallium (DTS) imaging (if unable to exercise) or stress dobutamine echo is recommended. If the ischemic area is small, surgery is permissible with recommended aggressive medical therapy management. If the ischemic area is moderate to large, with a suspicion of new or severe coronary stenosis, cardiac catheterization is recommended before the planned surgery. Also see Chapter 9, Section B.2, Figure 9.3.

An alternative view: McFalls et al. demonstrated the lack of benefit of perioperative revascularization of patients with significant but stable CAD; this will render the stress test and its low positive predictive value not useful in this patient. Considering the patient as high risk given all his comorbidities, adopting an aggressive perioperative medical treatment with β-blockers or α_2-blockers, statins and angiotensin inhibitors would be the alternative plan recommended.

Fleisher LA, Eagle KA. Clinical practice. Lowering cardiac risk in noncardiac surgery. *N Engl J Med.* 2001;345:1677–1682.

Fleisher LA, Beckman JA, Brown KA, et al. 2009 ACCF/AHA focused update on perioperative beta blockade incorporated into the ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation.* 2009;120: e169–e276.

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Slogoff S, Keats A. Myocardial ischemia revisited. *Anesthesiology.* 2006;105:214–216.

B.3. How would you classify the cardiac risk according to the type of surgery?

Surgery-specific cardiac risk of noncardiac surgery is related to two important factors: the type of surgery and the degree of hemodynamic stress associated with the procedure(s). The duration and intensity of coronary and myocardial stressors can be helpful in estimating the likelihood of perioperative cardiac events, particularly for emergency surgery. Surgery-specific risk for noncardiac surgery can be stratified as high, intermediate, and low.

- *High-risk* surgery (cardiac risk often >5%) includes major emergency surgery, particularly in the elderly; aortic and other major vascular surgery; peripheral vascular surgery; and anticipated prolonged procedures associated with large fluid shifts and/or blood loss.
- *Intermediate-risk* (cardiac risk generally <5%) procedures include carotid endarterectomy, head and neck surgery, intraperitoneal and intrathoracic, orthopedic, and prostate surgery. Endovascularly performed aortic stent procedures also are included in this category.
- *Low-risk* (cardiac risk generally <1%) procedures include endoscopic and superficial procedures, cataract surgery, and breast surgery.

Fleisher LA, Beckman JA, Brown KA, et al. 2009 ACCF/AHA focused update on perioperative beta blockade incorporated into the ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation.* 2009;120:e169–e276.

B.4. Are patients with a Q-wave infarction at greater risk for perioperative reinfarction than those with a non–Q-wave infarction?

Studies indicate that individuals who survive a non–Q-wave infarction are at greater risk for reinfarction than those who survive a Q-wave infarction. Patients who have not had a transmural wall infarction have a less extensive infarction and lower in-hospital mortality; however, they have a larger degree of jeopardized or at risk myocardium leading to a higher incidence of reinfarction or recurrent angina. This is in distinction to patients with complicated Q-wave infarctions who frequently do not survive the immediate postinfarction period but have a lower rate of reinfarction than non–Q-wave MI after this period. Theoretically, patients who have had a solitary coronary artery lesion and sustained a transmural infarction may be considered at a significantly lower risk for reinfarction as the area that was

at risk for ischemia is already necrotic. Although their risk of reinfarction may be low, there may be an increased risk of dysrhythmias because of the necrotic myocardium. It is important to remember (1) that the distinction between the Q- and non–Q-wave MI is an electrocardiographic classification and does not necessarily correlate with the pathologic findings of transmural and subendocardial infarctions; and (2) that there is overlap especially with the use of thrombolytic therapy.

Antman EM, Braunwald E. ST-elevation myocardial infarction: pathology, pathophysiology and clinical features. In: Zipes D, Libby P, Bonow R, et al., eds. *Braunwald's Heart Dsease, A Textbook of Cardiovascular Medicine*. 8th ed. Philadelphia: WB Saunders; 2008:1233–1300.

Landesberg G. Pathophysiology of perioperative myocardial infarction: facts and perspectives. *J Cardiothorac Vasc Anesth*. 2003;17:90–100.

Landesberg G, Beattie WS, Mosseri M, et al. Perioperative myocardial infarction. *Circulation*. 2009;119:2936–2944.

Priebe HJ. Perioperative myocardial infarction—aetiology and prevention. *Br J Anaesth*. 2005;95:3–19.

B.5. What is the role of exercise or pharmacologic stress test for this patient?

The aim of functional cardiovascular testing is to elicit evidence and severity of CAD by subjecting the heart to physiologic stress. Noninvasive diagnostic testing must be used judiciously. Ideally, testing should be accurate, add useful information to the overall risk assessment, and avoid unnecessary delays in surgery. Noninvasive tests of myocardial perfusion are classified by the type of stress applied to elicit transient and reversible ischemia or by the mode of detecting the ischemic area. Myocardial stress can be induced by exercise (e.g., treadmill, sitting or supine bicycle, or handgrip), by a pharmacologic agent that increases heart rate and myocardial contraction (e.g., dobutamine, atropine), or by a pharmacologic agent that can cause redistribution of coronary blood flow (e.g., dipyridamole, adenosine). Physiologic exercise provides an estimate of functional capacity, provides blood pressure and heart rate response, and detects myocardial ischemia through ST-segment changes. The accuracy of exercise ECG varies significantly among studies. Meta-analysis of the reported studies using treadmill testing in vascular surgery patients showed a rather low sensitivity (74%) and specificity (69%), comparable with daily clinical practice. The positive predictive value was as low as 10%, but the negative predictive value was very high (98%).

A significant fraction of the high-risk population cannot exercise to an adequate level and will require pharmacologic stress testing. During a stress test, an ischemic event might be suggested or detected by the patient's reporting of symptoms, appropriate ECG changes (horizontal or down-sloping ST-segment depression of 0.1 mV or ST elevation of 0.15 mV in two contiguous leads, reversible wall motion abnormalities on echocardiography, or reversible perfusion defects on radionuclide imaging with thallium or technetium.

The DTS and dobutamine stress echocardiography (DSE) before vascular surgery predict PMI or death, with a positive predictive value of only 12% to 14% and a negative predictive value of 88% and 94%, respectively. In one meta-analysis DSE tends to perform better than DTS. However, the large majority of the cited DTS involved older planar imaging technology that is no longer used. The low positive predictive value is expected because stress tests are designed to discover fixed coronary artery stenosis that exceed 70%. However, at least 50% of PMIs are due to plaque rupture, and it is often the noncritical, nonischemia-producing lesions that rupture.

Selection of the noninvasive stress test should be based primarily on patient characteristics, local availability, and expertise in interpretation. Because of simplicity, lower cost, and widespread familiarity with performance and interpretation, the standard low-level exercise ECG stress test remains the most reasonable test in patients who are able to exercise and have a resting ECG that is interpretable for ST-segment shifts. Patients with an ECG pattern that would interfere with interpretation of the ST segment (LBBB, pre-existing ST-segment abnormality in the precordial leads V_5 and V_6) should have an exercise test with imaging. Patients who are unable to exercise should have a pharmacologic stress test with imaging.

Dobutamine stress echocardiography is the preferred test if there is an additional question regarding valvular function or LV dysfunction.

Akhtar S. Ischemic heart disease. *Anesthesiol Clin.* 2006;24:461–485.

Akhtar S, Silverman D. Assessment and management of patients with ischemic heart disease. *Crit Care Med.* 2004;32(suppl):S126–S136.

Beattie WS. Evidence-based perioperative risk reduction. *Can J Anaesth.* 2005;52(suppl 1):R3.

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Kertai MD, Boersma E, Bax JJ, et al. A meta-analysis comparing the prognostic accuracy of six diagnostic tests for predicting perioperative cardiac risk in patients undergoing major vascular surgery. *Heart.* 2003;89:1327–1334.

Lustik S, Eichelberger J, Chhibber K. Preoperative stress testing: new guidelines. *J Clin Anesth.* 2004;14:375–380.

B.6. Would you discontinue any medication before surgery?

Patients with CAD are usually on a variety of medications. All antianginal drugs, especially β-blockers and statins, should be continued up to the time of surgery. Sudden withdrawal of antianginal drugs may produce rebound tachycardia and hypertension that may precipitate acute myocardial ischemia or infarction.

Current management of hypertensive patients suggests the continuation of antihypertensive therapy up to the day of surgery. In particular, β-blockers, calcium channel blocker, and nitrates should be continued. There is continued controversy about withholding angiotensin-converting enzyme inhibitors (ACE inhibitors) and angiotensin-2 receptor antagonist 24 hours prior to surgery. Prolonged hypotension has been observed in patients who are undergoing general anesthesia and who have chronically been treated with ACE inhibitors. Some recommend withholding ACE inhibitors for 24 hours prior to surgical procedures involving major body fluid shifts on significant blood loss. Hypotension attributed to ACE inhibitors is frequently responsive to fluid and/or administration or sympathomimetic drugs, such as phenylephrine and ephedrine. If hypotension is refractory to these measures, treatment with vasopressin or its long-acting analogue, terlipressin, may be effective.

Bertrand M, Godet G, Meersschaert K, et al. Should the angiotensin 2 antagonists be discontinued before surgery? *Anesth Analg.* 2001;92:26–30.

Fleisher LA, Beckman JA, Brown KA, et al. 2009 ACCF/AHA focused update on perioperative beta blockade incorporated into the ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation.* 2009;120:e169–e276.

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Tuman KJ, McCarthy RJ, O'Connor CJ, et al. Angiotensin-converting enzyme inhibitors increase vasoconstrictor requirements after cardiopulmonary bypass. *Anesth Analg*. 1995;88:7–17.

B.7. How would you premedicate this patient?

The patient with IHD should be adequately sedated before surgery to avoid anxiety-induced tachycardia and hypertension that may cause adverse myocardial ischemic events. Appropriate doses of a benzodiazepine may be given with the antianginal medications.

B.8. Is there a role for α_2-agonist in premedication?

α_2-agonists stimulate prejunctional alpha receptors and decrease norepinephrine release from prejunctional terminals, thereby decreasing noradrenergic central nervous system transmission, producing sedation, anxiolysis, and analgesia. Studies have shown that clonidine as a premedication reduces hypertension, tachycardia, and norepinephrine levels in patients undergoing aortic reconstruction. Clonidine also suppresses the normal postoperative increase in fibrinogen levels and antagonizes epinephrine-induced platelet aggregation. It has also been shown to decrease intraoperative myocardial ischemia. The more selective α_2-agonists, dexmedetomidine and mivazerol (IV form only available in Europe), also may reduce postoperative myocardial ischemia events in high-risk patients.

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Wjeysundera DN, Beattie WS, Naik JS. Alpha -2 adrenergic agonist to prevent perioperative cardiovascular complications: a meta-analysis. *Am J Med*. 2003;114:742–752.

C. Intraoperative Management

C.1. What are the intraoperative predictors for perioperative cardiac morbidity (PCM)?

Intraoperative predictors

Classic intraoperative predictors for perioperative MACE include emergency surgery, major vascular surgery, and prolonged (more than 3 hours) thoracic or upper abdominal surgery. Among the dynamic predictors, both hypotension and tachycardia predict PCM. Preoperative hypertension remains a controversial predictor. Most MIs occur early after surgery and are commonly associated with ST-segment depression. Prolonged duration of myocardial ischemia (>20 to 30 minutes or cumulative duration of >1 to 2 hours) seems to be the important factor associated with adverse cardiac outcome. Although LV end-diastolic pressure

is a sensitive measure of ischemia, studies report that pulmonary capillary wedge pressure is an insensitive indicator. Other factors associated with poor outcome are increased intraoperative bleeding/large quantity of blood transfusions and poor preoperative cardiac functional status.

Bui H, Haukoos J, Donayre C, et al. Predictors of cardiac morbidity and mortality in patients undergoing endovascular repair of the thoracic aorta. *Ann Vasc Surg.* 2004;18(1):22–25.

Mangano DT. Perioperative cardiac morbidity. *Anesthesiology.* 1990;72:153–184.

Priebe HJ. Perioperative myocardial infarction—aetiology and prevention. *Br J Anaesth.* 2005;95:3–19.

Sprung J, Abdelmalak B, Gottlieb A, et al. Analysis of risk factors for myocardial infarction and cardiac mortality after major vascular surgery. *Anesthesiology.* 2000;93(1):129–140.

C.2. How would you monitor the patient in the operating room?

The patient should be monitored using the following American Society of Anesthesiologist standard guidelines:

- *ECG*—simultaneous leads V_5 and II
- *Blood pressure*—noninvasive automatic Doppler sphygmomanometer and an invasive arterial catheter
- *Capnography*—to determine continuous end-tidal CO_2 analysis.
- *Pulse oximetry*—to assess arterial oxygenation
- *Oxygen analyzer*—to determine inspired fraction of oxygen.
- *Availability of esophageal/bladder temperature probe*—to determine temperature changes.

In addition to these monitors, this patient will also required the monitoring of urine output with a Foley catheter.

American Society of Anesthesiologists. ASA standards for basic anesthetic monitoring. ASA House of Delegates, Oct. 2005.

C.3. What ECG leads would you monitor? Why V_5?

ECG ST-segment changes are most commonly used for detection of intraoperative myocardial ischemia. Multiple-lead ECG monitoring provides the best clinically available method of detecting perioperative ischemia, primarily by combining leads II, V_3, V_4, and V_5 (II/V_5 detection of 80%, II/V_4, V_5 detection of 96%).

Landesberg et al. were able to correlate the duration of ischemia observed in the ST-segment analysis of a continuously monitoring 12-lead ECG throughout the perioperative period with the incidence of PMI. He also found that ischemia is transient even in patients who will develop an infarct.

Certain prerequisites must be met to use the ECG effectively:

- The diagnostic mode allows detection of ST-segment changes that are filtered out by the monitoring mode.
- The number of ECG leads and their location affects detection of ischemic events.
- Immediate availability of a hard copy of the ECG leads for more detailed analysis.
- Studies have reported that even trained observers recognize only 15% to 40% of electrocardiographic ischemic events displayed on oscilloscope.
- The introduction of ST-segment trending helps as an early warning detection system but should not replace examination of the ECG printout.

Fleisher LA. Real-time intraoperative monitoring of myocardial ischemia in non-cardiac surgery. *Anesthesiology.* 2000:92;1183–1188.

Landesberg G, Beattie WS, Mosseri M, et al. Perioperative myocardial infarction. *Circulation.* 2009;119:2936–2944.

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London MJ, Hollenberg M, Wong MG, et al. Intraoperative myocardial ischemia: localization by continuous 12-lead electrocardiography. *Anesthesiology.* 1988;69:232–241.

C.4. Would you use a pulmonary artery catheter (PAC)?

Right heart catheterization is not recommended for monitoring patients with intraoperative ischemia. Large observational study and a randomized multicenter trial did not show benefit associated with the use of right heart catheterization after major noncardiac surgery. A meta-analysis of randomized controlled trials showed that the use of PAC neither increased mortality or conferred any benefits to critically ill patients. A number of studies report that PAC is an insensitive monitor for myocardial ischemia and should not be inserted with this as a primary indication.

Fleisher LA, Beckman JA, Brown KA, et al. 2009 ACCF/AHA focused update on perioperative beta blockade incorporated into the ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation.* 2009;120:e169–e276.

Shah MR, Hasselblad V, Stevenson L, et al. Impact of pulmonary artery catheter in critically ill patients: meta-analysis of randomized control trials. *JAMA.* 2005;294(13):1664–1670.

C.5. Would you use transesophageal echocardiography (TEE) as a monitor?

TEE is a very sensitive diagnostic method of new onset myocardial ischemia. The echocardiographic diagnosis of myocardial ischemia is based on the development of new regional wall motion abnormalities, decreased systolic wall thickening, and ventricular dilation. Usually, a cross-sectional view (deep transgastric short axis), of the LV is imaged because this view displays the myocardial perfusion territories of the three major coronary arteries. TEE was found to be twice as predictive as ECG in identifying CABG patients who have an MI. In CABG patients, postbypass regional wall motion abnormalities were related to adverse clinical outcome.

However, practitioners should realize certain limitations of TEE. One, preintubation events are missed, as are the ischemic events that can occur frequently at the end of the surgery, when tachycardia and hypertension appear as part of the emergence from general anesthesia. Real-time intraoperative analysis of the TEE image is associated with a decreased accuracy of interpretation. The examination could divert the anesthesiologist's attention from more important clinical details. Despite numerous reports extolling the virtues of TEE as an ischemia monitor, Hollenberg et al. demonstrated little incremental value over the 12-lead ECG. Furthermore, wall motion abnormalities may be difficult to interpret in the presence of LBBB, ventricular pacing, atrial fibrillation, or right ventricular overload.

Notwithstanding TEE's limitations, ESC and the AHA guidelines recommend the use of TEE intraoperatively or perioperatively to determine the cause of an acute, persistent, and life-threatening hemodynamic abnormality (class IIa recommendation).

However, its use as an ischemia monitor in noncardiac surgery is less validated and may only be considered in patients at high risk for developing myocardial ischemia who undergo major noncardiac surgery (class IIb recommendation by ESC).

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Miller JP, Lambert S, Shapiro WA, et al. The adequacy of basic intra-operative transesophageal echocardiography performed by experienced anesthesiologists. *Anesth Analg*. 2001;92:1102–1110.

Poldermans D, Bax JJ, Boersma E, et al. Guidelines for pre-operative cardiac risk assessment and perioperative cardiac management in non-cardiac surgery: the Task Force for Preoperative Cardiac Risk Assessment and Perioperative Cardiac Management in Non-cardiac Surgery of the European Society of Cardiology (ESC) and endorsed by the European Society of Anaesthesiology (ESA). *Eur Heart J*. 2009;30:2769–2812.

Wenger MB, Herndon OW, Gaba DM. The effect of electronic record keeping and transesophageal echocardiography on task distribution, workload, and vigilance during cardiac anesthesia. *Anesthesiology*. 1997;87:144–155.

C.6. Is regional anesthesia better than general anesthesia for patients with cardiac disease?

A number of studies in patients with cardiac disease have compared the effects of regional versus general anesthetics on the incidence of perioperative infarction, dysrhythmias, and CHF. No distinct advantage is apparent between them when considering PCM and mortality in patients undergoing peripheral vascular surgery. There is some evidence to support regional anesthesia over general anesthesia in an effort to optimize graft patency if the regional technique is extended into the postoperative period to provide neuraxial analgesia. The choice of technique does not appear to affect mortality in patients requiring hip fracture surgery, although Urwin et al. reported, in a meta-analysis, decreased 1-month mortality and incidence of thromboembolic complications in patients receiving regional anesthesia for hip fracture repair. Epidural anesthesia also has been shown to promote quicker return of bowel function postoperatively when the catheter has been placed at T12 level or higher. Anastomotic (colon/bowel) breakdown in patients with epidural anesthesia/analgesia (secondary to hyperperistaltism) has rarely been reported. Most studies tend to show quicker return of bowel function when local anesthetics alone are administered epidurally. In summary, no one technique demonstrates a consistent advantage. The MASTER (Multicenter Australian Study of Epidural Anesthesia)

trial randomized 915 patients undergoing major abdominal surgery to receive either combined general and epidural anesthesia/epidural analgesia or general anesthesia with opioid analgesia. Epidural anesthesia/analgesia did not decrease death or cardiovascular outcomes, but modestly improved pulmonary outcomes compared with the general anesthesia group.

Randomized studies and a meta-analysis of several randomized clinical trials in noncardiac surgery patients, comparing outcome with regional and general anesthetic techniques have shown little consistent evidence of improved outcome and reduced postoperative morbidity and mortality. Thus, the current guidelines recommends that the choice of anesthesia is best left to the discretion of the anesthesia care team, which will consider the need for postoperative ventilation; pulmonary/neuromuscular comorbidities; cardiovascular effects, including myocardial depression; sympathetic blockade consequences; and dermatomal level of the procedure.

Bode RH Jr, Lewis KP, Zarich SW, et al. Cardiac outcome after peripheral vascular surgery: comparison of general and regional anesthesia. *Anesthesiology*. 1996;84:3–13.

Breen P, Park K. General anesthesia versus regional anesthesia. *Int Anesthesiol Clin*. 2002;40(1):61–71.

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Norris EJ, Beattie C, Perler BA, et al. Double-masked randomized trial comparing alternate combinations of intraoperative anesthesia and postoperative analgesia in abdominal aortic surgery. *Anesthesiology*. 2001;95:1054–1067.

Rigg JR, Jamrozik K, Myles PS, et al. Epidural anaesthesia and analgesia and outcome of major surgery: a randomised trial. *Lancet*. 2002;359:1276–1282.

Urwin SC, Parker MJ, Griffiths R. General versus regional anaesthesia for hip fracture surgery: a meta-analysis of randomized trials. *Br J Anaesth*. 2000;84:450–455.

C.7. How would you induce general anesthesia?

It is essential to prevent hypotension, hypertension, and tachycardia, which can precipitate myocardial ischemia. Different induction techniques may be employed to achieve this goal. For example, while the patient is being preoxygenated, fentanyl (up to 5 μg per kg) is given slowly to achieve drowsiness and to attenuate the sympathetic response to direct laryngoscopy and intubation of the trachea. Then, using lower doses of thiopental, propofol, or etomidate, unconsciousness is achieved. Succinylcholine or an intermediate duration nondepolarizing relaxant is administered to facilitate tracheal intubation. A few minutes before intubation the use of a short-acting β-blocker (esmolol) could help to further attenuate the sympathetic response to intubation if necessary. High-dose opioid-based anesthesia was previously popularized because of cardiovascular stability; however, because of the need for prolonged postoperative mechanical ventilation and ICU stay, this technique is no longer considered the technique of choice. On the other hand, in patients undergoing cardiac surgery, volatile anesthetics have been shown to decrease troponin release, enhance LV function compared with propofol, midazolam, or balanced anesthesia technique with opioids. The AHA guidelines extrapolate that data and recommend that it can be beneficial to use volatile anesthetic agents during noncardiac surgery for the maintenance of general anesthesia in hemodynamically stable patients at risk for myocardial ischemia.

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Martin DE, Rosenberg H, Aukburg SJ, et al. Low-dose fentanyl blunts circulatory responses to tracheal intubation. *Anesth Analg.* 1982;61:680.

Priebe HJ. Perioperative myocardial infarction—aetiology and prevention. *Br J Anaesth.* 2005;95:3–19.

C.8. Would you induce anesthesia with etomidate? Why?

Although etomidate has a negative inotropic effect on failing and nonfailing human heart muscle in doses that exceed the clinical dose, it appears to have a better hemodynamic profile than other commonly used induction agents, especially in the setting of coronary heart disease; with an induction dose of 0.2 to 0.3 mg per kg, there are minimal changes in heart rate, stroke volume, or cardiac output, and the blood pressure may decrease up to 15% because of decrease of systemic vascular resistance. Etomidate does suppress adrenocortical function, cause myoclonus, and prolong duration of seizure when used for electroconvulsive therapy.

Haessler R, Madler C, Klasing S, et al. Propofol/fentanyl versus etomidate/fentanyl for the induction of anesthesia in patients with aortic insufficiency and coronary artery disease. *J Cardiothorac Vasc Anesth.* 1992;6:173–180.

Sprung J, Ogletree-Hughes ML, Moravec CS, et al. The effects of etomidate on the contractility of failing and nonfailing human heart muscle. *Anesth Analg.* 2000;91:68–75.

Stoelting RK, Hillier SC. *Pharmacology and Physiology in Anesthetic Practice.* 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2006:155–179.

C.9. What is the best choice of anesthetic agents for maintenance of anesthesia? Why?

There appears to be no one best myocardial protective agent or technique. The knowledge of physiologic and pharmacologic effects of anesthetic agents in patients with cardiac disease will allow flexibility in their selection. The use of inhalation versus narcotic anesthesia in patients with cardiac disease is still debated, although the cardiovascular effects of both techniques and the physiologic differences between them are well documented. However, most outcome studies have not demonstrated a difference between the techniques. Studies of more than 3,000 noncardiac surgical patients with CAD have concluded that anesthetic type does not affect outcome.

Inhalation anesthetics are thought to possess ischemic preconditioning properties. Most investigations of anesthetic ischemic preconditioning have been done in patients undergoing cardiac surgery, but maybe there are potential beneficial effects in the high-risk cardiac patients undergoing noncardiac surgery. However, none of the trials to date were powered to evaluate MI or death as an outcome. The AHA guidelines extrapolate that data and recommend that it can be beneficial to use volatile anesthetic agents during noncardiac surgery for the maintenance of general anesthesia in hemodynamically stable patients at risk for myocardial ischemia (class IIa).

The use of nitrous oxide in patients with history of CAD has been questioned since the early 1990s, when animal and human studies showed the increase in peripheral vascular resistance, diastolic dysfunction, and subsequently myocardial

ischemia. Batner et al. demonstrated the increase on homocysteine plasma levels of patients during carotid endarterectomy when nitrous oxide was administered and the correlation of those levels with increase incidence of myocardial ischemia. A large multicenter study is currently under way to better define the harmful effects of nitrous oxide.

The objectives during maintenance are not dissimilar to any other patient: amnesia, unconsciousness, and analgesia. These goals are constrained by the hemodynamic effect of each agent in order to provide heart rate control, coronary pressure perfusion, and effects on LV function. The preferred anesthetic technique will be a balanced anesthetic approach: opioids, with low/moderate doses of volatile anesthetics and benzodiazepines. If the plan is to extubate the trachea at the end of surgery a high-dose/longer-acting narcotics should be avoided.

Badner NH, Beattie WS, Freeman D, et al. Nitrous oxide-induced increased homocysteine concentrations are associated with increased postoperative myocardial ischemia in patients undergoing carotid endarterectomy. *Anesth Analg.* 2000;91(5):1073–1079.

Beattie WS. Evidence-based perioperative risk reduction. *Can J Anaesth.* 2005;52(suppl 1):R3.

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Myles PS, Leslie K, Peyton P, et al. Nitrous oxide and perioperative cardiac morbidity (ENIGMA-II) Trial: rationale and design. *Am Heart J.* 2009;157:488–494.e1.

C.10. What muscle relaxant would you choose? Why?

The hemodynamic goals are to avoid hypotension, tachycardia, and hypertension. Intermediate-acting neuromuscular blocking agents such as vecuronium, cisatracurium, and rocuronium can be used safely because they produce minimally significant cardiovascular changes. A peripheral nerve stimulator should be used to monitor the degree of blockade.

Fleming N. Con: the choice of muscle relaxants is not important in cardiac surgery. *J Cardiothorac Vasc Anesth.* 1995;9:772–774.

Hudson RJ, Thomson IR. Pro: the choice of muscle relaxants is important in cardiac surgery. *J Cardiothorac Vasc Anesth.* 1995;9:768–771.

C.11. You notice a new 3-mm ST-segment depression in lead V_5. How would you treat it?

ST-segment depression can be an indicator of myocardial ischemia. Initial efforts should be focused on determining its etiology. Management of ischemia should include pharmacologic manipulation of the determinants of myocardial oxygen supply and demand.

The crucial aspect of such management includes the following:

- Heart rate control and adequate coronary perfusion pressure. If ST depression is associated with tachycardia and hypertension, the most common cause during surgery is inadequate anesthesia. Therefore, adequate levels of anesthesia should be achieved first. Heart rate control can also be achieved by the use of β-blockers. Caution should be exerted in patients with known contraindications and hemody-

namic instability. Calcium channel blockers (verapamil) can be used if β-blockers are contraindicated. The calcium channel blockers are considered the drug of choice if coronary spasm is suspected.

- Avoidance of hypotension and use of vasopressors to sustain coronary perfusion pressure.
- The use of nitrates is advocated as long as it does not compromise coronary perfusion pressure. Nitrates decrease myocardial oxygen demand by decreasing preload, intracavitary pressure, and myocardial tension. In addition, NTG increases the ratio of endocardial to epicardial blood flow.
- Oxygen delivery should be increased by correcting anemia and increasing the fraction of inspired oxygen.
- Oxygen demand also could be reduced by correction of hypothermia and/or shivering, if present.
- Secondary therapies should consider the use, if feasible, of antiplatelet therapy such as aspirin. If necessary, even intraoperative use of heparin can be considered, as long as it is not surgically contraindicated.

Fleisher LA, Beckman JA, Brown KA, et al. 2009 ACCF/AHA focused update on perioperative beta blockade incorporated into the ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation.* 2009;120:e169–276.

Priebe HJ. Perioperative myocardial infarction—aetiology and prevention. *Br J Anaesth.* 2005;95:3–19.

C.12. Would you give prophylactic intravenous NTG to prevent myocardial ischemia?

There are no randomized data that support the use of prophylactic intraoperative intravenous NTG in patients at high risk. NTG should be used only when ischemia is detected and the hemodynamic effects of other agents in use are considered.

Beattie WS. Evidence-based perioperative risk reduction. *Can J Anaesth.* 2005;52(suppl 1):R3.

Fleisher LA, Beckman JA, Brown KA, et al. 2009 ACCF/AHA focused update on perioperative beta blockade incorporated into the ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation.* 2009;120:e169–e276.

C.13. What is the significance of tight control of the heart rate intraoperatively?

Numerous studies have shown that intraoperative tachycardia and the duration of tachycardia could cause myocardial ischemia. Therefore, control of heart rate intraoperatively could significantly reduce the risk of perioperative myocardial events. It is clear that heart rate should be maintained to less than 100 beats per minute, however, the optimal heart rate for all patients has not be determined. Some recommend maintaining the heart rate between 60 to 70 beats per minute in high-risk patients.

Slogoff et al. in the 1980s were able to correlate tachycardia with the occurrence of intraoperative myocardial ischemia.

Raby et al. demonstrated that by identifying the high-risk patients, whose preoperative Holter tracing showed signs of ischemia, and controlling the heart

rate 20% below the ischemia threshold or approximately 60 beats per minute with esmolol, during vascular surgeries could reduce the risk of perioperative myocardial ischemia.

Feringa et al. demonstrated that tight heart rate control instead of just the use of β-blockers reduced perioperative myocardial ischemia and improved long-term outcome in vascular surgery patients.

Auerbach A, Goldman L. Assessing and reducing the cardiac risk of non-cardiac surgery. *Circulation.* 2006;113:1361–1376.

Beattie WS, Wijeysundera DN, Karkouti K, et al. Does tight heart rate control improve beta-blocker efficacy? An updated analysis of the non-cardiac surgical randomized trials. *Anesth Analg.* 2008;106:1039–1048.

Biccard BM, Sear JW, Foex P. Meta-analysis of the effect of heart rate achieved by perioperative beta-adrenergic blockade on cardiovascular outcomes. *Br J Anaesth.* 2008; 100:23–28.

Feringa H, Bax J, Boersma E, et al. High dose beta-blockers and tight heart rate control reduce myocardial ischemia and troponin T release in vascular surgery patients. *Circulation.* 2006;114:344–349.

Fleisher LA, Beckman JA, Brown KA, et al. 2009 ACCF/AHA focused update on perioperative beta blockade incorporated into the ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation.* 2009;120:e169–e276.

Landesberg G, Beattie WS, Mosseri M, et al. Perioperative myocardial infarction. *Circulation.* 2009;119:2936–2944.

Poldermans D, Boersma E, Bax J, et al. The effect of bisoprolol on perioperative mortality and myocardial infarction in high-risk patients undergoing vascular surgery. *N Engl J Med.* 1999;341:1789–1794.

Raby KE, Brull SJ, Timimi F, et al. The effect of heart rate control on myocardial ischemia among high-risk patients after vascular surgery. *Anesth Analg.* 1999;88:477–482.

Slogoff S, Keats A. Myocardial ischemia revisited. *Anesthesiology.* 2006;105:214–216.

C.14. When would you extubate the trachea in this patient? What could you do to prevent hypertension and tachycardia during extubation and emergence?

At the end of surgery, assuming no intraoperative complications, the trachea would be extubated when the patient is fully awake, breathing adequately, and neuromuscular blockade is fully reversed. To prevent tachycardia and hypertension associated with extubation and emergence, low doses of medications such as 1 mg per kg of lidocaine or esmolol, or 0.015 to 0.03 mg per kg of nicardipine, or 0.1 mg per kg of labetalol, diltiazem, or verapamil before emergence in order to reduce sympathetic response of emergence and extubation can be administered.

Atlee JL, Dhamee MS, Olund TL, et al. The use of esmolol, nicardipine, or their combination to blunt hemodynamic changes after laryngoscopy and tracheal intubation. *Anesth Analg.* 2000;90:280.

Fujii Y, Kihara S, Takahashi S, et al. Calcium channel blockers attenuate cardiovascular responses to tracheal extubation in hypertensive patients. *Can J Anaesth.* 1998;45:655–659.

Mikawa K, Nishina K, Maekawa N, et al. Attenuation of cardiovascular responses to tracheal extubation: verapamil versus diltiazem. *Anesth Analg.* 1996;82:1205–1210.

D. Postoperative Management

D.1. What are the postoperative predictors of PCM?

In noncardiac surgical patient, the highest risk of cardiac morbidity is in the postoperative period. It is during this period where up to 67% of the ischemic events occur. This period is characterized by increase in heart rate, blood pressure, sympathetic discharge, and hypercoagulability. Heart rate commonly increases postoperatively by 25% to 50% over intraoperative values, and tachycardia occurs in 10% to 25% of patients. Postoperative myocardial ischemia occurs in 27% to 41% of high-risk patients. Most of these events (50% or higher) are silent (without angina). Postoperative MI is usually preceded by prolonged ST-segment depression. This change on ECG is easily missed if not continuously monitored because most of the changes will revert completely to baseline in almost all cases. In patients with high or intermediate clinical risk, who have known or suspected CAD and who are undergoing high- or intermediate-risk surgical procedures, the procurement of ECGs at baseline, immediately after the surgical procedure, and daily on the first 2 days after surgery appears to be the most cost-effective strategy. PMI may be associated with tachycardia and pain. Studies involving large numbers of patients suggest that postoperative ischemia is the most important marker of immediate and long-term adverse cardiovascular events. It is associated with a 2.8-fold increase in the odds of all adverse cardiac outcomes.

The highest incidence of troponins elevation, a biochemical marker of ischemia, frequently occurs 8 to 24 hours after the surgical procedure; even mild elevations are associated with postoperative cardiac ischemia and they could help to categorize the short- and long-term risk of the surgical patient as they are independent predictors of mortality. Postoperative MI has also been associated with other clinical conditions as postoperative hypothermia, hypercoagulability, postoperative pain, and anemia.

Akhtar S. Ischemic heart disease. *Anesthesiol Clin.* 2006;24:461–485.

Landesberg G, Mosseri M, Shatz V, et al. Cardiac troponin after major vascular surgery. The role of perioperative ischemia, preoperative thallium scanning, and coronary revascularization. *J Am Coll Cardiol.* 2004;44:569–575.

Lee TH, Marcantonio ER, Mangione RC, et al. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. *Circulation.* 1999;100:1043–1049.

Le Manach Y, Perel A, Coriat P, et al. Early and delayed myocardial infarction after abdominal aortic surgery. *Anesthesiology.* 2005;102:885–891.

Priebe HJ. Perioperative myocardial infarction—aetiology and prevention. *Br J Anaesth.* 2005;95:3–19.

D.2. How would you control postoperative pain?

The postoperative period can be stressful due to the onset of pain during emergence from anesthesia, fluid shifts, temperature changes, and alteration of respiratory function. Marked changes occur in plasma catecholamine concentration, hemodynamics, ventricular function, and coagulation following noncardiac surgery, particularly in patients with pre-existing cardiac disease. These stressors place the patient at increased risk for development of adverse cardiac outcome. Effective pain management is essential to prevent adverse outcome. Intravenous patient-controlled analgesia and/or patient-controlled epidural analgesia are popular methods for reducing postoperative pain. Several studies suggest that effective pain management leads to a reduction in postoperative catecholamine surges and hypercoagulability. Norris et al. found that

using patient-controlled intravenous analgesia or patient-controlled epidural analgesia, the incidence of myocardial ischemia/infarction were comparable in patients undergoing abdominal aneurysm repair as long as the pain control and hemodynamics of the patients were similar.

Fleisher LA, Beckman JA, Brown KA, et al. 2009 ACCF/AHA focused update on perioperative beta blockade incorporated into the ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation.* 2009;120:e169–e276.

Mangano DT, Siliciano D, Hollenberg M, et al. Postoperative myocardial ischemia. Therapeutic trials using intensive analgesia following surgery. *Anesthesiology.* 1992;76:342–353.

Matot I, Oppenheim-Eden A, Ratro R, et al. Preoperative cardiac events in elderly patients with hip fracture randomized to epidural or conventional analgesia. *Anesthesiology.* 2003;98:156–163.

Norris EJ, Beattie C, Perler BA, et al. Double-masked randomized trial comparing alternate combinations of intraoperative anesthesia and postoperative analgesia in abdominal aortic surgery. *Anesthesiology.* 2001;95:1054–1067.

D.3. Is postoperative anemia associated with adverse cardiac outcome?

Patients with IHD may be adversely affected by anemia. Based on existing literature, the evidence is sufficient to state that transfusions are rarely beneficial if the Hgb level exceeds 10 g per dL (Hct >30%) in the absence of acute blood loss. It is also reasonable to state that the patient may benefit from a transfusion if the Hgb level falls below 7 g per dL. The controversy remains between Hgb concentrations of 8.0 to 10.0 g per dL.

Adverse clinical consequences of acute, iatrogenic, postoperative anemia has been demonstrated. Nelson et al. have identified a Hct of 28% as being the threshold associated with increased incidence of morbid cardiac events in postoperative vascular surgical patients. Wu et al. also demonstrated the benefit of higher Hgb levels in patients with acute myocardial infarction (MI). However, the TRICC trial (Transfusion Requirement in Critical Care) was not able to demonstrate a significant difference in 30-day mortality between patients who were "liberally" transfused (average Hgb, 10.7 g per dL) versus the restrictive group (no transfusion unless Hgb <7 g per dL). Rao et al. published the data from the combination of three large randomized trial stating the risk of death is 3.9 times greater in patients who were transfused compared with those who did not. The controversy remains, however, when confronted with high-risk patients or those who demonstrate myocardial ischemia, we are more likely to transfuse packed cells to raise the Hct to 30%.

Beattie WS, Karkouti K, Wijeysundera DN, et al. Risk associated with preoperative anemia in noncardiac surgery: a single-center cohort study. *Anesthesiology.* 2009;110:574–581.

Hebert PC, Wells G Blaichman MA, et al. Transfusion requirement in critical care investigators, Canadian Critical Care Trial Group. *N Engl J Med.* 1999;340:409–417.

Nelson AH, Fleisher LA, Rosenbaum SH. Relationship between postoperative anemia and cardiac morbidity in high-risk vascular patients in the intensive care unit. *Crit Care Med.* 1993;21:860.

Rao SV, Jolllis JG, Harrington RA, et al. Relationship of blood transfusion and clinical outcomes in patients with acute coronary syndromes. *JAMA.* 2004;292:1555–1562.

Wu WC, Rathore SS, Wang Y, et al. Blood transfusion in elderly patients with acute myocardial infarction. *N Engl J Med.* 2001;345:1230–1236.

D.4. Is postoperative hypothermia associated with postoperative myocardial ischemia?

Hypothermia is common during anesthesia and surgery owing to anesthetic-induced inhibition of thermoregulatory control. The principal initial cause of hypothermia is core-to-peripheral redistribution of body heat.

Perioperative hypothermia is associated with numerous complications; it triples the incidence of adverse myocardial outcomes in high-risk patients, increases blood loss. Even mild hypothermia has been associated with an increased incidence of wound infection following colon resection. Also, it adversely affects oxygen availability in tissues, changes the kinetics and action of some anesthetic agents and muscle relaxants, and is associated with delayed postanesthetic recovery.

Core hypothermia may increase circulating catecholamines levels, leading to tachycardia, hypertension, systemic vasoconstriction, and an imbalance between oxygen demand and supply. Frank et al. studied 100 patients undergoing lower extremity vascular surgery. They found that unintentional hypothermia (sublingual temperature less than 35°C [95° F]) on arrival to postoperative intensive care unit (ICU) is associated with a significantly higher incidence of myocardial ischemia (36% vs. 13%), angina (18% vs. 15%), and Pao_2 less than 80 mm Hg (52% vs. 30%) during the early postoperative period. Therefore, aggressive warming and heat conservation are mandatory during and after surgery. It is recommended to continue forced-air warming for the first several hours after surgery in hypothermic patients.

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Frank SM, Beattie C, Christopherson R, et al. The Perioperative Ischemia Randomized Anesthesia Trial Study Group. Unintentional hypothermia is associated with postoperative myocardial ischemia. *Anesthesiology.* 1993;78:468–476.

Frank SM, Fleisher LA, Breslow MJ, et al. Perioperative maintenance of normothermia reduces the incidence of morbid cardiac events. A randomized clinical trial. *JAMA.* 1997;277:1127–1134.

Leslie K, Sessler D. Perioperative hypothermia in the high-risk surgical patient. *Best Pract Res Clin Anesthesiol.* 2003;17:485–498.

Priebe HJ. Perioperative myocardial infarction—aetiology and prevention. *Br J Anaesth.* 2005;95:3–19.

D.5. How would you make a diagnosis of perioperative myocardial infarction (PMI)?

The definition of MI, according to the World Health Organization, is based on elevation of biomarkers, in conjunction with cardiac symptoms, ECG changes, or echocardiographic changes.

Most ischemic episodes occur after and not during the operation: This is probably because of the high postoperative stresses related to anesthesia and surgery. Several studies have examined the optimal method for diagnosing a PMI. Clinical symptoms (mostly asymptomatic), postoperative ECG changes (even analysis of serial basal ECGs is limited in its sensitivity to new PMI, because most infarctions are non–Q wave in nature), and elevation of the MB fraction of creatine kinase (CK-MB) have been most extensively studied. Cardiac-specific enzyme elevations such as troponin I (cTn I), troponin T (cTn T) are currently the standard of care for biochemical diagnosis of a PMI because they demonstrate sensitivity and tissue specificity superior to other available biomarkers.

In the purest physiologic sense, any detectable necrosis is an acute myocardial infarction; however, troponin elevation can be observed in many other conditions in which the heart is stressed. Even small elevations of specific markers of myocardial damage, such as cardiac troponins, should be acknowledged as indicative of myocardial injury. From a clinical perspective, there is clear evidence that any amount of detectable cardiac troponin release is associated with an increased risk of new adverse cardiac events.

The increased sensitivity of troponins to myocardial injury that is not normally sufficient to cause CK-MB elevation, chest pain, or electrocardiographic abnormalities has been shown. Landesberg et al. reported a good correlation between duration of ischemia and the rise in cardiac-specific troponin I and is an area of active research. Many investigators would agree that the increase in cardiac troponins postoperatively, even if no cardiovascular signs and symptoms are present, carries poor long-term outcome.

Clinicians need to be sensitive to redundancy in testing. Some authors have demonstrated that routine cardiac troponin monitoring is an easy, effective, and inexpensive way to detect postoperative myocardial injury. However, the ACC/AHA guidelines reserves the use of this biomarkers for patients at high risk and those with clinical, ECG, or hemodynamic evidence of cardiovascular dysfunction. At best, there is still lack of agreement regarding who should be tested. Routine measurement of postoperative troponins in asymptomatic or low-risk patients undergoing low risk procedure is not warranted.

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D.6. How would you manage the patient with a suspected PMI?

There is lack of control-evidence regarding management of PMI in the postsurgical patient. PMI could include three different clinical scenarios/diagnosis: unstable angina (UA), non–ST-elevation myocardial infarction (NSTEMI), and ST-elevation myocardial infarction (STEMI).

The initial management should focus on the following diagnosis:

- Evaluation of chest pain if present.
- 12-Lead ECG and determination of changes, if present.
- Measurement of biomarkers of cardiac injury. A cardiac-specific troponin is the preferred marker.
- Immediate consultation of a cardiologist and risk stratification to determine high-risk patients.

It is important to consider the recent surgical procedure and consultation with the surgical team regarding impact of aspirin and antithrombin therapy.

Unless a contraindication exists, patients with an acute coronary syndrome of the type UA or NSTEMI should be treated with oxygen, aspirin (acetylene salicylic acid), sublingual/intravenous NTG for chest pain relief, as long as blood pressure is adequate, a β-blocker, antithrombin therapy (unfractionated heparin or low molecular weight heparin), and/or a GP IIb/IIIa inhibitor.

The cardiology consultant should guide further management:

- Option one is a routine angiographic approach, in which coronary angiography and revascularization are performed unless a contraindication exists. Within this approach, the most common strategy advocates for a period of medical stabilization. A more aggressive approach calls for coronary angiography and revascularization performed within 24 hours of the onset of symptoms or diagnosis; the rationale for the more aggressive approach is the protective effect of carefully administered antithrombin and antiplatelet therapy on reperfusion procedures outcome.
- The alternative approach, commonly referred to as the initially conservative strategy, is guided by ischemia, with angiography reserved for patients with recurrent ischemia or a "high-risk" stress test despite medical therapy.

Regardless of the angiographic strategy, an assessment of LV function (echocardiography, ventriculogram, or nuclear ventriculography) should be strongly considered because of the importance of treating patients who have impaired LV function with ACE inhibitors, β-blockers and, surgical revascularization (CABG) when appropriate (e.g., three-vessel disease).

If the patient presents with a STEMI, recognized on the basis of the 12-lead ECG, the management will be initially similar to UA/NSTEMI (oxygen, acetylene salicylic acid, NTG, β-blockers), then one should attempt to complete restoration of flow in the infarct artery by pharmacologic means (fibrinolysis: usually contraindicated after a surgical procedure due to the increased risk of bleeding), PCI (balloon angioplasty with or without deployment of an intracoronary stent under the support of pharmacologic measures to prevent thrombosis), or surgical measures (CABG).

Evidence supports expeditious restoration of flow in the obstructed infarct artery after the onset of symptoms in patients with STEMI as a key determinant of short- and long-term outcomes regardless of whether reperfusion is accomplished by fibrinolysis or PCI. Early reperfusion of ischemic myocardium within the risk region of an occluded infarct-related artery interrupts the occurring necrosis, reduces ultimate infarct size, preserves regional and global ventricular function, and improves survival. A subset of patients will have severe three-vessel or left main disease or anatomic features unfavorable for PCI and may be candidates for urgent or emergency CABG.

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SECTION III

The Gastrointestinal System

CHAPTER 14

Intestinal Obstruction

Joseph Tjan

A 73-YEAR-OLD WOMAN

with an acute abdomen was scheduled to undergo an emergency exploratory laparotomy. She complained of severe abdominal pain with periodic bouts of bilious vomiting. Past surgical history included a right hemicolectomy for colon cancer. Blood pressure 85/60 mm Hg, pulse of 115 beats per minute, and hematocrit of 45%.

A. Medical Disease and Differential Diagnosis

1. What is the differential diagnosis of the acute abdomen?
2. What are the causes of intestinal obstruction of the small bowel and of the large bowel?
3. Differentiate between simple and strangulated bowel obstruction.
4. Is it important to differentiate whether the bowel obstruction is located in the small bowel or large bowel? Why?
5. What are the signs and symptoms of intestinal obstruction?
6. What are the causes and effects of bowel distention?
7. Describe the fluid shifts during small bowel intestinal obstruction.
8. Discuss the systemic derangements that occur with intestinal obstruction.
9. Can there be actual losses of red cell mass?
10. What is an ileus? Discuss its causes and treatment.
11. What are the systemic effects from the absorption of bacteria and bacterial products?

B. Preoperative Evaluation and Preparation

1. Is it important to decompress the abdomen before surgical intervention? Why?
2. Describe the respiratory implications.
3. What are the implications of the tense abdominal wall?
4. Outline the methods of abdominal decompression.
5. Discuss the goals of fluid management.
6. What would you use as a guide to fluid volume replacement?

C. Intraoperative Management

1. What dangers are present during induction? How are they planned for?
2. Does the administration of antacids and/or histamine-2 (H_2) blockers before the induction of anesthesia have a significant value in patients with small bowel obstruction?
3. In what position would you intubate this patient? Would you use Sellick maneuver?
4. Is succinylcholine the best muscle relaxant to use for the rapid-sequence induction?
5. Would you remove or leave the nasogastric tube (NGT) in place before inducing anesthesia?
6. Would you use nitrous oxide in this patient?
7. Are there any benefits to using a high concentration of inspired oxygen?

D. Postoperative Management

1. What are the principles of postoperative care in this patient?
2. Are there any postoperative respiratory problems associated with factors other than aspiration?
3. If the patient did aspirate gastric contents, what are the possible sequelae of this event? What is the treatment?
4. What is gram-negative sepsis? Describe the clinical picture and treatment.

A. Medical Disease and Differential Diagnosis

A.1. What is the differential diagnosis of the acute abdomen?

Intestinal obstruction accounts for approximately 15% to 20% of hospitalized patients with an acute abdomen. Abdominal pain can be divided into three categories: visceral, somatic, and referred. Visceral pain is transmitted through the autonomic nervous system through C fibers located intramurally in hollow viscera and in the capsule of abdominal organs. Visceral pain is dull, crampy, or aching in nature, and the factors that produce it include stretching and distention that result in increased wall tension, inflammation, ischemia, torsion, compression, and certain chemicals. Transmission of somatic pain occurs through A-δ fibers of spinal nerves to produce pain that is characteristically sharp, severe, and persistent. Somatic pain is caused by irritation of the parietal peritoneum and arises as a response to acute changes in pH or temperature, as seen with bacterial or chemical inflammation. Referred pain is that which is felt in a region of the body different from the point of its origin because of the sharing of common pathways for afferent neurons arising from different sites. A proper history and physical examination with early diagnosis is of utmost importance in the management of the patient with an acute abdomen. In a recent review of over 1,100 patients with abdominal pain who presented to the emergency room, the most common diagnosis overall was nonspecific abdominal pain. Appendicitis, intestinal obstruction, urologic disorders, and gallstones were the most common surgical causes in order of decreasing

frequency. In 47% of the patients, surgical intervention was required. The gastrointestinal and intraperitoneal causes of abdominal pain are listed in Table 14.1. There are many extraperitoneal causes of abdominal pain, and these include pulmonary, cardiac, neurologic, metabolic, toxic, infectious, vascular, and hematologic conditions.

Brunicardi FC, ed. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010: 980–1001.

Table 14.1 Gastrointestinal and Intraperitoneal Causes of Abdominal Pain

I. Inflammation/infection
- A. Peritoneum
  - 1. Chemical and nonbacterial peritonitis–perforated peptic ulcer, gallbladder, ruptured ovarian cyst, mittelschmerz
  - 2. Bacterial peritonitis
    - a. Primary peritonitis–pneumococcal, streptococcal tuberculous
    - b. Perforated hollow viscus–stomach, intestine, biliary tract
- B. Hollow intestinal organs
  - 1. Appendicitis
  - 2. Cholecystitis
  - 3. Peptic ulceration
  - 4. Gastroenteritis
  - 5. Regional enteritis
  - 6. Meckel's diverticulitis
  - 7. Colitis–ulcerative, bacterial, amebic
  - 8. Diverticulitis
- C. Solid viscera
  - 1. Pancreatitis
  - 2. Hepatitis
  - 3. Hepatic abscess
  - 4. Splenic abscess
- D. Mesentery
  - 1. Lymphadenitis
- E. Pelvic organs
  - 1. Pelvic inflammatory disease
  - 2. Tuboovarian abscess
  - 3. Endometritis

II. Mechanical (obstruction, acute distention)
- A. Hollow intestinal organs
  - 1. Intestinal obstruction–adhesions, hernia, tumor, volvulus, intussusception
  - 2. Biliary obstruction–calculi, tumor, choledochal cyst, hematobilia
- B. Solid viscera
  - 1. Acute splenomegaly
  - 2. Acute hepatomegaly–cardiac failure, Budd-Chiari syndrome
- C. Mesentery
  - 1. Omental torsion
- D. Pelvic organs
  - 1. Ovarian cyst
  - 2. Torsion or degeneration of fibroid
  - 3. Ectopic pregnancy

III. Vascular
- A. Intraperitoneal bleeding
  - 1. Ruptured liver
  - 2. Ruptured spleen
  - 3. Ruptured mesentery
  - 4. Ruptured ectopic pregnancy
  - 5. Ruptured aortic, splenic, or hepatic aneurysm
- B. Ischemia
  - 1. Mesenteric thrombosis
  - 2. Hepatic infarction–toxemia, purpura
  - 3. Splenic infarction
  - 4. Omental ischemia

IV. Miscellaneous
- A. Endometriosis

From Schwartz SI, Shires GT, Spencer FC, et al., eds. *Principles of Surgery.* 7th ed. New York: McGraw-Hill;1999:1036, with permission.

A.2. What are the causes of intestinal obstruction of the small bowel and of the large bowel?

Intestinal obstruction can be of extraluminal (e.g., adhesions, hernias, or carcinomatosis); intraluminal (e.g., gallstones or foreign bodies); or intramural (e.g., Crohn disease or tumors) origin. The term *mechanical bowel obstruction* denotes an actual physical barrier that interferes with the normal progression of intestinal contents. The most common cause of small bowel obstruction is postoperative adhesions, followed by incarcerated hernias and malignant tumors. Postoperative adhesions make up approximately 75% of cases of small bowel obstruction. Alternatively, neoplasms account for most large bowel obstruction. Other causes of large bowel obstruction include diverticulitis and volvulus.

Brunicardi FC, ed. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:980–1001, 1015–1057.

A.3. Differentiate between simple and strangulated bowel obstruction.

Simple obstruction occurs when the lumen is obstructed and the blood supply remains normal. Occlusion of the blood supply to the obstructed bowel results in a strangulated obstruction. Toxic fluid is discharged into the bowel lumen, bowel wall, and peritoneal cavity when venous outflow obstruction occurs. It is important to recognize strangulation preoperatively because the implications are more serious and the mortality rate is high at between 8% and 25%. Conversely, the mortality rate for nonstrangulating bowel obstruction is under 5%. A closed-loop obstruction is present when both limbs of the loop are obstructed. This leads rapidly to strangulation, occasionally even before clinical evidence of intestinal obstruction appears.

Brunicardi FC, ed. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:980–1001.

A.4. Is it important to differentiate whether the bowel obstruction is located in the small bowel or large bowel? Why?

Yes. Simple mechanical obstruction of the small bowel results in altered bowel motility, bowel distention with progressive accumulation of fluid and gas, and systemic derangements. If the obstruction is not relieved promptly, strangulation ensues, leading to bowel necrosis and the leakage of blood, fluid, and toxic substances into the bowel and peritoneal cavity. Approximately 60% to 80% of intestinal obstructions occur in the small bowel.

Although the signs and symptoms may be similar, large bowel obstruction is usually more insidious than small bowel obstruction. Except for a volvulus, large bowel obstruction has less of a propensity to strangulate. The colon is essentially a storage organ and has little secretory and absorptive functions. Therefore, systemic derangements are less severe with large bowel obstruction. The most important complication is progressive distention and rupture of the colon, especially in the presence of a competent ileocecal valve. The cecum is the usual site of rupture.

Brunicardi FC, ed. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:980–1001, 1015–1057.

A.5. What are the signs and symptoms of intestinal obstruction?

The four cardinal signs and symptoms of intestinal obstruction are crampy abdominal pain, nausea and vomiting, obstipation, and abdominal distention. Intestinal activity initially increases in an effort to overcome the obstruction, leading to colicky pain and diarrhea. The colicky pain often is diffuse and alternates with quiescent periods. The duration of the quiescent period depends on the site of intestinal obstruction. With a high obstruction, the duration is approximately 4 to 5 minutes, and with lower ileal obstruction, the duration is 15 to 20 minutes. Steady, severe abdominal pain usually indicates strangulation.

Vomiting commonly occurs immediately after the onset of bowel obstruction, followed by a variable quiescent period before recurrence. Vomiting becomes more frequent and bilious the higher the level of obstruction, and, with the exception of a volvulus, it is uncommon in colonic obstruction. Abdominal distention is a late finding that may be absent in high small bowel obstruction that is associated with frequent bouts of emesis. Other signs of intestinal obstruction include localized tenderness, fever, tachycardia, and leukocytosis. White blood cell counts of 15,000 to 25,000 per μL is strongly suggestive of strangulation, but this is not a sensitive test because 40% of patients with strangulation have normal white blood cell counts. The presence of acidosis also will increase the likelihood of strangulation. With the development of dehydration, serum chemistries will change, hemoconcentration occurs, and urine output will diminish and become concentrated.

A partial bowel obstruction is more likely to be present if the patient is able to pass stool and/or gas 6 to 12 hours after the onset of symptoms.

The most important initial diagnostic procedures are plain x-ray films of the abdomen in the supine and upright positions with upright and lateral chest x-ray films. In intestinal obstruction, gas–fluid levels are seen on the radiographs. Although normal within the stomach and colon, intestinal gas is usually minimal and infrequent in the small bowel. Therefore, gas–fluid levels are indicative of obstruction but also may be seen in gastroenteritis, severe constipation, sprue, and severe aerophagia. The radiologic findings and those features that differentiate simple mechanical obstruction from an ileus are summarized in Table 14.2.

Brunicardi FC, ed. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:980–1001.

Table 14.2 Radiologic Signs in Intestinal Obstruction

SIGN	SIMPLE MECHANICAL OBSTRUCTION	ADYNAMIC ILEUS
Gas in intestine	Large bow-shaped loops in ladder pattern	Copious gas diffusely through intestine
Gas in colon	Less than normal	Increased, scattered through colon
Fluid levels in intestine	Definite	Often very large throughout
Tumor	None	None
Peritoneal exudate	None	Present with peritonitis; otherwise absent
Diaphragm	Somewhat elevated; free motion	Elevated: diminished motion

From Schwartz SI, Shires GT, Spencer FC, et al., eds. *Principles of Surgery*. 7th ed. New York: McGraw-Hill;1999:1061, with permission.

A.6. What are the causes and effects of bowel distention?

Intestinal obstruction results in the sequestration of fluid and gas within the bowel lumen proximal to the site of obstruction. Accumulation of fluid accounts for most of the bowel distention. As intraluminal pressure increases, the secretory function of the bowel increases progressively. Prostaglandin release seems to mediate this hypersecretion of fluid. In addition, reabsorption is impaired once intraluminal pressure exceeds 20 cm H_2O. The basic composition of the intestinal gas is that of swallowed air. As bowel distention continues from the ongoing gas and fluid accumulation, intraluminal and intramural pressures rise. The increased intramural pressures lead to progressive interference with the mesenteric blood supply, resulting in a strangulated obstruction with its associated morbidity and mortality.

Brunicardi FC, ed. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:980–1001.

A.7. Describe the fluid shifts during small bowel intestinal obstruction.

Normally, approximately 7 to 9 L of fluid are secreted daily into the upper gastrointestinal tract. The secretions include saliva (500 to 2,000 mL); gastric juice (1,000 to 2,000 mL);, bile (300 to 600 mL); pancreatic juice (300 to 800 mL); and succus entericus (2,000 to 4,000 mL) (Table 14.3). Because of small intestinal reabsorption, only 400 mL passes the ileocecal valve.

In small bowel obstruction, several mechanisms contribute to fluid and electrolyte loss. The most important is the accumulation of fluid in the bowel lumen because the obstructed bowel becomes overly secretory instead of absorptive. Sequestration of fluid within the bowel wall accounts for the edematous appearance of the bowel. This, in turn, results in free peritoneal fluid because of transudation of fluid across the serosal surface of the bowel. Fluid accumulation above the obstruction can be remarkable. In early small bowel obstruction, 1,500 mL of fluid accumulates in the bowel. Once intestinal obstruction is well established and vomiting occurs, 3,000 mL of fluid may be present. When the patient exhibits hypotension and tachycardia, indicating circulatory instability, as much as 6,000 mL of fluid is in the abdomen. Lastly, vomiting and/or nasogastric suctioning further increase fluid losses.

Table 14.3 Volume and Composition of Gastrointestinal Fluids

	24-HOUR VOLUME (mL)	NA^+ (mEq/L)	K^+ (mEq/L)	CL^- (mEq/L)	HCO_3^- (mEq/L)
Saliva	500–2,000	2–10	20–30	8–18	30
Stomach	1,000–2,000	60–100	10–20	100–130	0
Pancreas	300–800	135–145	5–10	70–90	95–120
Bile	300–600	135–145	5–10	90–130	30–40
Jejunum	2,000–4,000	120–140	5–10	90–140	30–40
Ileum	1,000–2,000	80–150	2–8	45–140	30
Colon	—	60	30	40	—

From Miller RD, ed. *Miller's Anesthesia*. 6th ed. New York: Churchill Livingstone;2005:1788, with permission.

Brunicardi FC, ed. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010: 980–1001.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010: 1723–1735.

A.8. Discuss the systemic derangements that occur with intestinal obstruction.

The systemic derangements that occur can be categorized as follows: hemodynamic changes, electrolyte abnormalities, and disturbances in acid–base balance.

Hemodynamically, if fluid and electrolyte losses are not corrected, central venous pressure will fall. Hypotension and tachycardia will follow as the vascular volume decreases in relation to the size of the vascular bed. The shock state develops as the body calls forth sympathomimetic amines to increase cardiac output and decrease the size of the vascular bed.

Small bowel obstruction results in the loss of vast quantities of isotonic extracellular fluid. The extent of extracellular fluid loss may be monitored by serial hematocrit determinations. A rise in the hematocrit is proportionate to the amount of fluid loss. For example, if the hematocrit has risen to 55%, approximately 40% of plasma and extracellular fluid volume has been lost.

As the obstruction continues, there is a gradual decrease in the plasma sodium and chloride concentrations. Hyponatremia will aggravate hypovolemic hypotension, and confusion and somnolence will ensue. Hypokalemia will be manifested in delayed ventricular conduction, ST-T segment changes, and ventricular arrhythmias. With respect to acid–base balance, the most common occurrence is metabolic acidosis because of the effects of dehydration, starvation, ketosis, and loss of alkaline secretions. Metabolic alkalosis is rare and is the result of marked loss of acidic gastric fluid. Monitoring includes serial determinations of sodium, potassium, chloride, and carbon dioxide.

Brunicardi FC, ed. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:980–1001.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. New York: Churchill Livingstone; 2010:1723–1735.

A.9. Can there be actual losses of red cell mass?

Yes. In long-standing intestinal obstruction, especially when it is associated with strangulation, increased permeability of the bowel wall occurs with loss of red cells into the bowel and peritoneal cavity. Whole blood or packed cells may be needed to restore circulating red blood cells.

Brunicardi FC, ed. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:980–1001.

A.10. What is an ileus? Discuss its causes and treatment.

An ileus is a functional failure of normal aboral intestinal transit. Except for the discomfort of abdominal distention, it is usually not painful. The pathogenesis of ileus is poorly understood, but stimulation of the inhibitory adrenergic neurons may play an important role. Classification of ileus is as follows:

- *Adynamic or inhibition ileus*—diminished or absent motility from neuromuscular inhibition

- *Spastic ileus*—contracted bowel musculature with resultant uncoordinated motility
- *Ileus of vascular occlusion*—disordered motility secondary to ischemia

Adynamic ileus is the most common form because it is present following every intra-abdominal operation. Postoperative ileus affects different parts of the gastrointestinal tract differently. Small bowel function recovers within 24 hours, whereas gastric motility may take 24 to 48 hours to return. The colon is the most severely affected, where an ileus may persist for as long as 3 to 5 days.

If postoperative ileus is prolonged, other contributing causes should be sought that include:

- *Metabolic*—hypokalemia, hyponatremia, hypomagnesemia
- *Drugs*—narcotics, antacids, anticoagulants, phenothiazines, ganglionic blockers
- *Other*—intraperitoneal inflammation (e.g., acute appendicitis or acute pancreatitis), sepsis, hematoma, wound infection, ureteral colic, spine or rib fractures, basal pneumonia

Spastic ileus is rare and occurs with heavy metal poisoning, porphyria, and uremia. Management of ileus involves treatment of the underlying cause, nasogastric decompression, intravenous hydration, correction of metabolic abnormalities, and nutritional support if needed. No specific drug therapy has been shown to be effective.

Brunicardi FC, ed. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:980–1001.

A.11. What are the systemic effects from the absorption of bacteria and bacterial products?

The normal mucosa is impermeable to bacteria and toxins produced by bacterial degradation, but permeability is affected when there is impairment of the blood supply in a strangulated segment of bowel. Intestinal obstruction also can lead to a change in the bacterial flora within the bowel. Subsequent transperitoneal absorption of bacteria and toxins can result in bacteremia and septic shock.

Brunicardi FC, ed. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:980–1001.

B. Preoperative Evaluation and Preparation

B.1. Is it important to decompress the abdomen before surgical intervention? Why?

Yes, because of the respiratory and circulatory complications that ensue.

Brunicardi FC, ed. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:980–1001.

B.2. Describe the respiratory implications.

The distended bowel produces pressure on the diaphragm, limiting its downward movement, and resulting in inadequate ventilation and an increased work of breathing in a patient who already may be malnourished. The decrease in tidal volume and the

reduction in functional residual capacity (FRC) result in a low Pao_2 and an elevated $Paco_2$. It is especially true if the stomach also is distended. An additional reason for gastric decompression is to remove fluid and air from the stomach to lessen the likelihood of aspiration of gastric contents into the tracheobronchial tree during the induction of anesthesia. A long-standing obstruction and its associated respiratory compromise will result in a gasping, dusky, cyanotic, semicomatose patient.

Brunicardi FC, ed. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:980–1001.

B.3. What are the implications of the tense abdominal wall?

The first is related to the higher incidence of reverse peristalsis. Second, the stretched abdominal wall requires deeper anesthesia and more muscle relaxant to provide adequate operating conditions. These implications may increase morbidity. The distended abdomen significantly affects venous return by two mechanisms. First, distention decreases negative intrathoracic pressure and thereby decreases venous return. The second is due to direct vena caval compression from intraperitoneal tension. In long-standing intestinal obstruction, a large volume of intraperitoneal fluid may be present in the abdominal cavity. At the time of surgical incision, care must be taken to prevent the fluid from escaping rapidly from the abdomen to minimize severe hypotension. As fluid is slowly released from the abdominal cavity, the blood pressure should be checked frequently and the rate of fluid release adjusted to minimize a fall in blood pressure.

Brunicardi FC, ed. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:980–1001.

B.4. Outline the methods of abdominal decompression.

There are two types of tubes available for abdominal decompression: short tubes placed in the stomach and long tubes placed in the small intestine. To reduce the likelihood of regurgitation of gastric contents, it is important that the stomach be empty before induction of anesthesia. This is best done by the sump tube, which is more efficient than the simple Levin tube. The sump tube is composed of a double lumen, one for aspiration and the other to allow air into the stomach. The Miller-Abbott tube is a long intestinal tube that is initially passed into the stomach, and an incorporated balloon containing mercury at its tip aids in its passage through the pylorus into the small bowel.

Although gastric and intestinal tubes are employed to relieve abdominal distention, they do not function solely as definitive therapy for bowel obstruction except in postoperative ileus, partial small bowel obstruction, and intestinal obstruction resulting from inflammation that is expected to subside with conservative therapy. For all other bowel obstructions, the mainstay of therapy remains surgical intervention.

Brunicardi FC, ed. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:980–1001.

B.5. Discuss the goals of fluid management.

Estimating the degree of fluid deficit in intestinal obstruction is extremely difficult and often underestimated. There is significant sequestration of fluid within the bowel

lumen, bowel wall, and transudation into the peritoneal cavity. Poor preoperative nutrition and protein loss into the bowel may lead to hypoalbuminemia and further fluid losses. The primary goal of fluid management is the initial restoration of intravascular volume to a state of normovolemia. This will lead to the optimization of oxygen delivery to the tissues and organs. The second goal is the correction of electrolyte disturbances, including acid–base derangements, which may exist. Because the fluid lost to an obstructed segment of bowel is similar to plasma in composition, a balanced salt solution such as lactated Ringer's solution is appropriate to use for fluid resuscitation.

Brunicardi FC, ed. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:980–1001.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. New York: Churchill Livingstone; 2010:1723–1735.

B.6. What would you use as a guide to fluid volume replacement?

Fluid losses can be calculated knowing that the body turns over 17 to 18 L of fluid a day, made up of intestinal secretions, urine excreted by the kidneys, fluid loss through the feces, and insensible losses from the lungs and skin. As mentioned previously, there is tremendous fluid loss into the gut, which may amount to 4,500 to 9,000 mL of functional fluid loss, including loss resulting from vomiting and nasogastric suctioning. If there is significant bowel wall edema and leakage of fluid into the peritoneal cavity because of peritonitis, an additional 7 L of fluid may be sequestered in the peritoneal space. Measurement of central venous pressure, hourly urine output, arterial blood pressure, heart rate, and skin turgor can be used to guide fluid replacement. In addition, there must be ongoing modifications in the management of fluid and electrolytes to achieve the desired physiologic goals.

Brunicardi FC, ed. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:980–1001.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. New York: Churchill Livingstone; 2010:1723–1735.

C. Intraoperative Management

C.1. What dangers are present during induction? How are they planned for?

Regurgitation of stomach contents and subsequent aspiration into the tracheobronchial tree is the principal danger during induction of anesthesia for the patient with intestinal obstruction.

Mortality associated with aspiration of gastric contents ranges widely from 3% to 70%. Abdominal surgery in particular has been associated with up to 75% of the perioperative mortality resulting from aspiration pneumonitis. The incidence of aspiration for all anesthetics is almost 5 per 10,000 anesthetics. A rapid sequence induction intubation (RSI) has been traditionally recommended. An awake intubation might be preferred if a difficult intubation is anticipated.

For awake intubation, the patient's lips, tongue, and pharynx should be sprayed with a topical anesthetic. Care must be taken to avoid anesthetizing the larynx because the defense mechanism for laryngeal closure will be lost in the event that regurgitation or vomiting should occur. Therefore, a superior laryngeal nerve block or a transtracheal injection is not warranted in these patients. Sedation should be limited or avoided altogether.

RSI assumes the completion of tracheal intubation with a cuffed endotracheal tube to occur in the shortest possible time from the period of loss of consciousness. Intuitively, this should decrease the risk of aspiration. Scientific evidence fails to support it. A meta-analysis of 184 clinical trials failed to show a decrease in pulmonary aspiration of gastric contents following RSI. According to Sellick, cricoid pressure if applied, should not be released until the cuff is inflated and correct placement of the endotracheal tube has been verified by measures including auscultation and capnometry. There is growing controversy on usefulness of cricoid pressure itself. Cricoid pressure is associated with an increased rate of failed intubation. Radiologic studies have shown that the esophagus is displaced laterally rather than occluded in over 50% of cases and reflex relaxation of the lower esophageal sphincter (LES) in response to cricoid pressure may provoke regurgitation. Observational studies have shown that cricoid pressure is frequently applied incorrectly and it is difficult to clinically teach application of 40 N of pressure. Should the patient remain hemodynamically unstable following fluid and electrolyte resuscitation, ketamine or etomidate is preferable for induction of anesthesia.

Brimacombe JR, Berry AM. Cricoid pressure. *Can J Anaesth.* 1997;44:414–425.

Gobindram A, Clarke S. Cricoid pressure: should we lay off the pressure? *Anaesthesia*. 2008;63:1258–1259.

Miller RD, ed. *Miller's Anesthesia.* 7th ed. New York: Churchill Livingstone; 2010:1585–1608.

Neilipovitz DT, Crosby ET. No evidence for decreased incidence of aspiration after rapid sequence induction. *Can J Anaesth.* 2007;54:748–764.

Salem MR, Bruniga KW. Cricoid pressure decreases lower sphincter esophageal tone. *Anesthesiology.* 2008;109:806–810.

Sellick BA. Cricoid pressure to control regurgitation of stomach contents during induction of anesthesia. Preliminary communication. *Lancet.* 1961;2:404–406.

Smith KJ, Dobranowski J, Yip G, et al. Cricoid pressure displaces the esophagus; An observational study using magnetic resonance imaging. *Anesthesiology.* 2003;99:60–64.

C.2. Does the administration of antacids and/or histamine-2 (H_2) blockers before the induction of anesthesia have a significant value in patients with small bowel obstruction?

The volume and pH of gastric contents and the presence or absence of particulate matter appear to be the three most important factors for determining the degree of pulmonary injury following aspiration. The classical term *at risk* is thought to imply a gastric volume greater than 25 mL with a pH less than 2.5. Approximately 40% of emergency surgical patients have a gastric pH below 2.5. The more critical factor involved in determining the degree of lung injury appears to be the pH of gastric contents. Therefore, outcomes are better with aspirations of large volumes of nonacidic material compared with that of small volumes of acidic material. Normally, clear, nonparticulate antacids (0.3 M sodium citrate) are effective in raising gastric pH and, likewise, H_2 blocking agents are effective in reducing gastric volume and acidity. However, because of the large volumes of fluid sequestered in the bowel, antacids and/or H_2 blockers have little or no value in high mechanical intestinal obstruction. When there is time to prepare the patient, these agents may be of some value in partial small bowel obstruction to reduce both gastric volume and acidity.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia.* 6thed. Philadelphia: Lippincott Williams & Wilkins; 2009:589–591.

Miller RD, ed. *Miller's Anesthesia.* 7th ed. New York: Churchill Livingstone; 2010:1605–1606.

C.3. In what position would you intubate this patient? Would you use Sellick maneuver?

Because gravity will aid in keeping gastrointestinal contents within the stomach, the head-up position is likely to decrease the incidence of regurgitation and thereby lessen the risk of pulmonary aspiration. Some clinicians advise that the patient be intubated in the supine position for fear that if the patient did vomit and was in the sitting or semisitting position, there would be a greater tendency to aspirate. However, we believe the head-up position is preferable. Should massive reverse peristalsis and regurgitation occur, vigorous suctioning and the head-down position are the best methods of preventing soilage of the tracheobronchial tree. The head-down position must be at least 10 degrees to prevent aspiration into the lungs.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1221–1224.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. New York: Churchill Livingstone; 2010:1605–1606.

C.4. Is succinylcholine the best muscle relaxant to use for the rapid-sequence induction?

Succinylcholine is still the only ultrarapid onset/ultrashort duration muscle relaxant for use in the rapid-sequence induction technique despite the known complications associated with the use of this drug. Several studies have appeared advocating the use of large doses of nondepolarizing muscle relaxants for rapid-sequence induction of anesthesia using the priming principle. The technique recommends the use of a small dose of a nondepolarizing muscle relaxant (usually about 20% of the ED95), followed 2 to 4 minutes later by a second intubating dose. These authors claim that patients can be intubated significantly earlier, by approximately 30 to 60 seconds, than if they are given a single intubating dose of a nondepolarizing muscle relaxant. With use of the priming principle, tracheal intubation can be achieved approximately 90 seconds following the second intubating dose of muscle relaxant. However, some argue that 90 seconds is not fast enough for a rapid-sequence induction technique, and furthermore, intubating conditions at 90 seconds may not be as ideal as that achieved at 60 seconds following succinylcholine administration. In addition, one should keep in mind that large doses of nondepolarizing muscle relaxants will result in a longer duration of neuromuscular blockade and may increase the potential for side effects. Another consideration of the priming technique that is especially relevant to the bowel-obstructed patient is the risk of aspiration due to the variable degree of neuromuscular blockade produced by the priming dose. See Table 14.4 for the priming dose and intubating dose of various muscle relaxants.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. New York: Churchill Livingstone; 2010:862–884.

C.5. Would you remove or leave the nasogastric tube (NGT) in place before inducing anesthesia?

The decision whether to remove or leave the NGT in place before induction of general anesthesia is somewhat controversial. The case for leaving the NGT in is that it allows gastric decompression, reduces intragastric pressure, and thereby reduces the chances of regurgitation. However, the presence of NGT during induction does not reliably ensure an empty stomach but renders the LES incompetent by preventing complete closure of the LES. The LES usually is 2 to 3 cm long and functions as the major impediment to reflux of gastric contents into the esophagus. An incompetent LES will increase the likelihood of regurgitation and aspiration of gastric contents into the tra-

Table 14.4 Rapid Tracheal Intubation[a] with Succinylcholine or Nondepolarizing Relaxants[b]

DRUG	PRIMING DOSE[c] (mg/kg)	INTUBATING DOSE[d] (mg/kg)	CLINICAL DURATION[e]	FULL RECOVERY[f]
Succinylcholine	None	1.0	5–10	12–15
Succinylcholine	Nondepolarizer pretreatment	1.5	5–10	12–15
Rapacuronium (ORG 9487)	None	1.5–2.0	15–30	35–55
Rocuronium	None	0.6–1.0	30–60	60–120
Mivacurium	0.02	0.25–0.3	15–20	25–35
Vecuronium	0.01	0.2	60–75	90–120
Vecuronium	None	0.3–0.4	90–150	120–180
Cisatracurium	0.01	0.25	55–75	75–100
Cisatracurium	None	0.4	75–100	100–120

[a] Intubation within 60 to 90 seconds following injection of the intubating dose of the relaxant.
[b] The administration of adequate dosage of intravenous anesthetic is assumed.
[c] This dose is given as preoxygenation is begun.
[d] This dose is given 2 to 4 minutes following the priming dose. For atracurium and mivacurium, slower injection (30 seconds) is recommended to minimize circulatory effects.
[e] Minutes from injection of the intubating dose to recovery of twitch to 25% of control.
[f] Minutes from injection of the intubating dose to recovery of twitch to 95% of control and train-of-four of 0.70.
From Miller RD, ed. *Anesthesia.* 5th ed. New York: Churchill Livingstone; 2000:427, with permission.

cheobronchial tree. Further, an indwelling NGT also may interfere with visualization of the larynx during laryngoscopy and endotracheal intubation.

Atlee JL, ed. *Complications in Anesthesia.* 2nd ed. Philadelphia: WB Saunders; 2007.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia.* 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1221–1224.

C.6. Would you use nitrous oxide in this patient?

Nitrous oxide should be avoided because its administration is associated with an undesirable increase in intraluminal gas volume and pressure that may lead to detrimental consequences. The blood-to-gas partition coefficient of nitrous oxide is 34 times that of nitrogen. Therefore, nitrous oxide in the blood can enter gas-filled cavities 34 times more rapidly than nitrogen can leave those cavities to enter the blood. When this happens during abdominal surgery, bowel distention will occur. The amount of distention will depend on the amount of gas already within the bowel and the duration of nitrous oxide administration. Normally, the bowel contains approximately 100 mL of gas that is mostly swallowed air, and nitrous oxide use results in a slow increase in bowel distention and intraluminal pressure. However, with bowel obstruction, the volume of gas within the bowel is greatly increased. Under these conditions, the increased intraluminal pressure associated with nitrous oxide administration may lead to bowel ischemia and necrosis. More commonly, it will cause difficulties with abdominal closure at the conclusion of surgery. Therefore, anesthesia should be maintained with oxygen, air and a volatile agent, and increments of opioids and muscle relaxants as needed.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1226–1227.

C.7. Are there any benefits to using a high concentration of inspired oxygen?

It has been suggested that administration of a high concentration of inspired oxygen may lead to a reduction in the incidence of surgical wound infections. Wound infections are serious complications of surgery that can prolong hospitalization, thereby increasing morbidity and medical costs. The factors that may play a role in producing surgical wound infections include the site and complexity of surgery, the tissue oxygen tension, the presence of any underlying illness, prophylactic antibiotic use, the intravascular volume status, the patient's body temperature, and postoperative pain control. Compared with the administration of 30% inspired oxygen, those patients receiving 80% inspired oxygen had approximately half the number of postoperative surgical wound infections in one study, however others have failed to reproduce these results. Timely use of prophylactic antibiotics and maintainence of normothermia in the perioperative period probably are more effective in decreasing surgical site infections.

Greif R, Akca O, Horn EP, et al. Supplemental perioperative oxygen to reduce the incidence of surgical wound infection. *N Engl J Med*. 2000;342:161–167.

D. Postoperative Management

D.1. What are the principles of postoperative care in this patient?

The principles of postoperative management are the same as those in the preoperative care of the patient, namely fluids and electrolytes, antibiotics, and gastrointestinal decompression. In the immediate postoperative period, there continues to be significant ongoing fluid loss, mostly secondary to "third spacing." However, this fluid loss gradually diminishes over time and usually by about the third postoperative day reverses in direction as fluid is transferred back into the vascular compartment. The significant autoinfusion that ensues must, therefore, be accounted for in the computations of the daily fluid requirements of the patient. Otherwise, congestive failure may follow, especially because patients with intestinal obstruction are often older adults with limited reserves in several organ systems. As electrolyte loss continues postoperatively, serial determinations of serum sodium and potassium levels may be necessary. Hyponatremia and hypokalemia are factors that contribute to prolonged postoperative ileus. Because return of normal intestinal motility usually is prolonged after surgical relief of bowel obstruction, abdominal decompression often must be continued for 5 or 6 days postoperatively, whereas bowel function returns on about the third postoperative day after a routine abdominal operation. Finally, postoperative management also may include frequent monitoring of hemodynamic parameters, hemoglobin concentration, and urine output.

Brunicardi FC, ed. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:980–1001.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. New York: Churchill Livingstone; 2010:2783–2802.

D.2. Are there any postoperative respiratory problems associated with factors other than aspiration?

The postoperative respiratory problems are those related to hypoventilation. Although the intestinal obstruction has been relieved, there still may be significant abdominal distention that will inhibit diaphragmatic motion, and the patient may develop hypoxia and hypercarbia. In addition, abdominal pain and the residual effects of inhaled anesthetics, intravenous anesthetics, and neuromuscular blockers may contribute to respiratory inadequacy. The 15% to 20% reduction in FRC associated with general anesthesia continues into the postoperative period and following upper abdominal surgery; vital capacity remains abnormal for more than a week. In summary, several pulmonary changes occur, including reductions in the following parameters: tidal volume, vital capacity, FRC, residual volume, and forced expiratory volume in 1 second (FEV_1). For these reasons, the endotracheal tube may be left in place to decrease anatomic dead space and make it possible to ventilate the patient during the immediate postanesthesia period. Leaving the endotracheal tube in place also is desirable for those patients with previous respiratory disease or in the morbidly obese individual. In both of these situations, the respiratory support will decrease residual atelectasis in the basilar portions of the lung. This will decrease any pulmonary shunt and lessen the need for a high inspired oxygen concentration (FIO_2). For those patients not requiring ventilatory support, a T-piece attached to the endotracheal tube will increase the FIO_2 to maintain the PaO_2 at an acceptable level. As the patient gradually regains respiratory adequacy (as shown by measuring inspiratory force and vital capacity), ventilation returns to normal and the patient can be safely extubated.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. New York: Churchill Livingstone, 2010:2879–2897.

D.3. If the patient did aspirate gastric contents, what are the possible sequelae of this event? What is the treatment?

Aspiration of gastric contents produces a chemical pneumonitis characterized initially by hypoxemia, bronchospasm, and atelectasis. In addition, the patient may exhibit signs of tachypnea, tachycardia, coughing, cyanosis, and shock. Arterial hypoxemia is the earliest and most reliable sign of aspiration. Even saline, when aspirated, causes significant hypoxemia.

Destruction of pneumocytes, lung parenchyma, and pulmonary microvasculature ensues, resulting in decreased surfactant activity, interstitial and alveolar edema, alveolar hemorrhage, and pulmonary hypertension (which results from hypoxic pulmonary vasoconstriction). The clinical picture may resemble that of adult respiratory distress syndrome. Radiographic findings are variable and may not appear for several hours. In at least 10% of cases, the radiographic films are normal. Positive findings usually consist of diffuse infiltrates bilaterally located in either the perihilar or basal regions.

Once vomiting or regurgitation occurs, immediate lateral head positioning, vigorous suctioning, and the head-down position should be instituted. To avoid disseminating the aspirated material further distally, the trachea is suctioned before beginning positive pressure ventilation. Bronchoscopy is indicated only for those patients who have aspirated solid material resulting in significant airway obstruction. Use of bronchial irrigation with saline or sodium bicarbonate solution is of little value and may actually be more detrimental than beneficial. Management includes keeping the patient intubated and well ventilated, following arterial blood gases, and obtaining serial chest x-ray films. Depending on the arterial blood gases, regulation of the inspired oxygen concentration and the amount of ventilation to maintain PaO_2 and

$Paco_2$ within normal limits will be necessary. If the fraction of inspired oxygen (Fio_2) has to be maintained above 60%, the use of positive end-expiratory pressure may be necessary to recruit additional alveoli and improve oxygenation. The best positive end-expiratory pressure will have the least effect on venous return and at the same time allow Fio_2 to be reduced to a safe level (40% or lower), thereby decreasing the likelihood of oxygen toxicity. It is important to realize that, although a patient may look well and have a clear chest without rhonchi or wheezes in the immediate postanesthetic period following aspiration, respiratory distress still may develop. It may take as long as 6 to 12 hours before the syndrome becomes manifest. The patient should be observed closely over 24 to 48 hours for the development of aspiration pneumonitis. Corticosteroid therapy remains controversial and the routine use of prophylactic antibiotics is not recommended because it may alter the normal flora of the respiratory tract and promote colonization by resistant organisms. However, antibiotics should be administered to those patients who show clinical signs of a secondary bacterial pulmonary infection with positive Gram stain and cultures or to those patients known to have aspirated gross fecal material, as with lower intestinal obstruction.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1433–1434.

D.4. What is gram-negative sepsis? Describe the clinical picture and treatment.

Gram-negative sepsis frequently leads to a shock state caused by endotoxins from the cell walls of gram-negative bacteria circulating in the blood. The earliest signs of a gram-negative infection include an elevated temperature above 101° F (38.33° C), the development of shaking chills, mild hyperventilation, respiratory alkalosis, and an altered sensorium. The hemodynamic abnormalities of gram-negative sepsis are not understood clearly but seem to follow two distinct hemodynamic patterns, depending on the patient's volume status.

The first is a hyperdynamic circulatory pattern associated with early septic shock that occurs in patients who are normovolemic before the onset of sepsis. These patients present with hypotension, high cardiac output, normal or increased blood volume, normal or high central venous pressure, decreased peripheral resistance, warm and dry extremities, hyperventilation, and respiratory alkalosis. However, in a patient who is hypovolemic before the onset of sepsis as with a strangulated obstruction of the small bowel, a hypodynamic pattern is seen characterized by hypotension; low cardiac output; high peripheral resistance; low central venous pressure; and cold, clammy extremities. Both types of patterns will have a better outcome if early treatment is begun, but if therapy is delayed or unsuccessful, cardiac and circulatory failure ensues associated with a low, fixed cardiac output and a resistant metabolic acidosis.

Definitive therapy of gram-negative sepsis includes the administration of appropriate antibiotics and early surgical debridement or drainage of the source of infection when indicated. Supportive measures are provided by fluid replacement and the use of vasoactive drugs. Corticosteroid administration as part of the treatment regimen for sepsis is still a controversial issue. Direct arterial blood pressure monitoring and insertion of a pulmonary artery catheter may be necessary for proper management.

Brunicardi FC, ed. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:102–110, 128–129.

Goldman L, Ausiello D, eds. *Cecil Textbook of Medicine*. 23rd ed. Philadelphia: WB Saunders; 2008:755–763.

CHAPTER 15

Liver Transplantation

VIVEK K. MOITRA

A 66-YEAR-OLD WOMAN

with a history of alcoholic cirrhosis and portal hypertension is admitted to the intensive care unit with altered mental status and low urine output. She has ascites and encephalopathy. Her kidney injury is acute with a creatinine clearance of 30 mL per minute. Her international normalized ratio (INR) is 3.0. Her hemoglobin level is 10.2 g per dL. She has a model for end-stage liver disease (MELD) score of 28 points. Her respiratory rate is 30 breaths per minute. She is scheduled for orthotopic liver transplantation.

A. Medical Disease and Differential Diagnosis

1. What are the potential graft options for liver transplantation?
2. What are the indications and contraindications for liver transplantation?
3. What is acute liver failure (ALF)?
4. What is the MELD score and how is it used in liver transplantation evaluation?
5. Describe the cardiovascular system of patients with end-stage liver disease (ESLD).
6. What causes acute kidney injury (AKI) in patients with cirrhosis?
7. What causes hyponatremia in patients with cirrhosis?
8. Discuss the neurologic manifestations of acute and chronic liver disease.
9. Why do patients with ESLD have abnormalities of hemostasis?
10. What is the differential diagnosis for hypoxemia in patients with cirrhosis?
11. What is portal hypertension? What are the sequelae of portal hypertension?

B. Preoperative Evaluation and Preparation

1. What preoperative workup is desirable?
2. How is ascites managed preoperatively?
3. How is hyponatremia managed preoperatively?
4. What is a transjugular intrahepatic portosystemic shunt (TIPS) procedure? What is the role of TIPS in the management of patients with ESLD?

5. How are hepatic encephalopathy and elevated intracranial pressure (ICP) treated?
6. Should this patient be transfused with fresh frozen plasma prior to surgery?

C. Intraoperative Management

1. What monitors would you use? Why?
2. What are the considerations for the induction of anesthesia?
3. How does liver disease affect intraoperative medication management?
4. What happens during the first stage (preanhepatic phase) of the liver transplant operation?
5. What happens during the second stage (anhepatic phase) of the liver transplant operation?
6. What physiologic disturbances should be anticipated during the second stage (anhepatic phase) of the liver transplant operation?
7. What is venovenous bypass? What are potential advantages and disadvantages of this procedure?
8. What surgical techniques are used to anastomose the donor and recipient inferior vena cava?
9. What are the potential advantages of the "piggyback" (vena cava preservation) technique?
10. What hemodynamic changes are expected after removal of vascular clamps? What is postreperfusion syndrome?
11. How would you treat hyperkalemia?
12. Why should you anticipate hypocalcemia?
13. What happens during the third stage of the liver transplant operation?
14. What causes intraoperative bleeding during each phase of liver transplantation? How is coagulopathy monitored and treated? What is thromboelastography (TEG)?
15. What are the complications of massive transfusion?
16. How are the complications of massive transfusion prevented?
17. How is hyperfibrinolysis managed?
18. When is intraoperative renal replacement therapy indicated?
19. What intraoperative signs suggest that the hepatic graft is working?

D. Postoperative Management

1. What are the goals of immediate postoperative care of the liver transplant patient?
2. What postoperative findings suggest that the hepatic graft is functioning?
3. What coagulation disturbances should be anticipated in the postoperative period?
4. Can renal function change after liver transplantation?
5. What vascular and biliary complications occur after liver transplantation?
6. What immunosuppressive agents will be given after liver transplantation? What are the major side effects?

A. Medical Disease and Differential Diagnosis

A.1. What are the potential graft options for liver transplantation?

Liver grafts are harvested from deceased or living donors. Cadaveric livers are procured after brain or cardiac death. Because of an increasing number of patients who

die waiting for a transplant, efforts to expand the donor pool include donation after cardiac death (DCD); harvesting marginal organs from cadavers with extended donor criteria; and procuring partial livers from living donors. DCD is the fastest growing source of transplant organs in the United States. Upon cardiac death (defined as the irreversible cessation of circulatory and respiratory function), the liver is harvested after a mandatory waiting period of 1 to 5 minutes. Warm ischemic time begins when the waiting period starts and ends when the liver is flushed with cold preservative solution. Transplantation of a DCD-donor liver that has been exposed to a longer warm ischemic time than a graft from a brain-dead donor may be associated with perioperative complications because of the organ's functional quality. Ideal organs have shorter warm and cold ischemic times and are harvested from hemodynamically stable donors younger than 50 years of age who are free of hepatobiliary or renal disease, infection, and cancer.

Extending donor criteria (age greater than 65 years; DCD; positive viral serology; split-liver; hypernatremia; or prior carcinoma, steatosis, or high-risk behaviors) to harvest organs with initial poor function or primary nonfunction expands the donor pool.

A related or unrelated healthy individual may donate a portion of the liver for transplantation. Usually, the right hepatic lobe is removed from a healthy individual and transplanted into an adult recipient. Transplantation of the smaller left hepatic lobe into pediatric or very small adults may decrease the incidence of complications in the donor. This chapter focuses on cadaveric liver transplantation into adult recipients.

Jeon H, Lee S. Living donor liver transplantation. *Curr Opin Organ Transplant*. 2010;15:283–287.

Reich DJ, Hong JC. Current status of donation after cardiac death liver transplantation. *Curr Opin Organ Transplant*. 2010;15:316–321.

Renz JF, Kin C, Kinkhabwala MD, et al. Utilization of extended donor criteria liver allografts maximizes donor use and patient access to liver transplantation. *Ann Surg*. 2005;242:556–565.

A.2. What are the indications and contraindications for liver transplantation?

Patients with acute liver failure (ALF), decompensated cirrhosis, or hepatocellular carcinoma are candidates for liver transplantation. In the United States, alcoholic liver disease is the most common cause of end-stage liver disease (ESLD), but cirrhosis from hepatitis C is the most common indication for orthotopic liver transplant. Specific indications for transplantation include recurrent cholangitis in patients with primary sclerosing cholangitis or intractable pruritus in patients with primary biliary cirrhosis. Uncommon indications for liver transplantation include hepatic tumors such as carcinoid tumors and hepatic adenoma; metabolic disorders such as alpha-1-antitrypsin deficiency; vascular disorders such as Budd-Chiari syndrome; cystic fibrosis; hemochromatosis; amyloidosis; sarcoidosis; and adult polycystic liver disease. Biliary atresia is the most common indication for pediatric liver transplantation.

Most surgeons will not offer transplantation to patients with severe cardiopulmonary or neurologic disease, significant hemodynamic instability, sepsis, extrahepatic malignancy, active alcohol or drug use, or unfavorable psychosocial circumstances. The decision to offer transplantation considers age and infection with human immunodeficiency virus.

Murray KF, Carithers RL Jr. American Association for the Study of Liver Diseases (AASLD) practice guidelines: evaluation of the patient for liver transplantation. *Hepatology*. 2005;41:1407–1432.

A.3. What is acute liver failure (ALF)?

In the absence of transplantation, ALF leads to death. ALF is defined by the absence of chronic liver disease, acute hepatitis (elevation in transaminases with an elevation in INR), encephalopathy, and illness less than 26 weeks. The most common causes of ALF are acetaminophen toxicity (39%), indeterminate (17%), idiosyncratic (13%), and acute viral hepatitis (12%, usually hepatitis B). Other etiologies include drugs (phenytoin and halothane), autoimmune disease, Wilson disease, Budd-Chiari syndrome, HELLP syndrome (hemolysis, elevated liver enzymes, low platelet count), acute fatty liver of pregnancy, toxins (i.e., trichloroethylene and tetrachloroethane in cleaning solvents and sniffed glue), and *Amanita phalloides*, the "death-cap" mushroom that grows wild in parts of the United States.

Bernal W, Auzinger G, Dhawan A, et al. Acute liver failure. *Lancet*. 2010; 376:190–201.

Steadman RH, Van Rensburg A, Kramer DJ. Transplantation for acute liver failure: perioperative management. *Curr Opin Organ Transplant*. 2010;15:368–373.

Stravitz RT, Kramer AH, Davern T, et al. Intensive care of patients with acute liver failure: recommendations of the U.S. Acute Liver Failure Study Group. *Crit Care Med*. 2007; 35:2498–2508.

A.4. What is the MELD score and how is it used in liver transplantation evaluation?

Grafts from deceased donors are offered to patients with the highest risk of death. Since 2002, the Model for End-stage Liver Disease (MELD), a validated and widely used prognostic tool that estimates disease severity and 3-month survival in patients with chronic liver disease, prioritizes organ allocation (Fig. 15.1). The MELD score ranges from 6 to 40 points and is calculated from the patient's serum bilirubin, serum creatinine, and INR.

Formula 15.1

MELD Score = 11.2 × ln (INR) + 9.57 × ln (creatinine, milligrams per deciliter) + 3.78 × ln (bilirubin, milligrams per deciliter) + 6.43 (an intercept). The score is rounded to the nearest whole number.

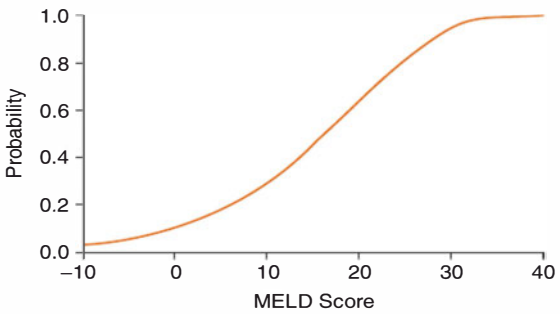

Figure 15.1 Relation between MELD score and 3-month mortality in patients with cirrhotic liver disease. MELD, model for end-stage liver disease. (From Wiesner RH, McDiarmid SV, Kamath PS, et al. MELD and PELD: application of survival models to liver allocation. *Liver Transplant*. 2001;7:567–580.)

There is a lower limit of 1 for all variables.

The maximum creatinine value is 4 mg per dL. For patients who receive dialysis, creatinine is set to 4 mg per dL.

Patients with a high score rank high on the transplant list and have a greater short-term risk of dying from liver disease than patients with lower scores. The incorporation of hyponatremia, an important prognostic factor in patient with cirrhosis, into the MELD score may provide better calibration and discrimination of the risk of death among patients awaiting liver transplantation.

Exceptions to the MELD classification exist for patients with fulminant hepatic failure and life expectancy of less than 7 days without a liver transplant. These patients are classified as *status 1* and rank highest on the waiting list. This group includes patients who develop ALF without a history of liver disease, suffer from primary graft nonfunction or hepatic artery thrombosis within 7 days of a liver transplant, or have acutely decompensated Wilson disease. Special case exceptions also exist for patients with diagnoses such as hepatocellular carcinoma.

Pediatric patients less than 12 years of age are ranked on the transplant waiting list according to the Pediatric End-Stage Liver Disease model. The pediatric end-stage liver disease score is similar in derivation to the MELD, but incorporates bilirubin, INR, albumin, age, and growth failure into the formula.

Laboratory values less than 1 are set to 1 to calculate a MELD score. The maximum serum creatinine considered within the MELD score equation is 4 g per dL. For patients receiving dialysis, creatinine is set to 4 mg per dL.

Kim WR, Biggins SW, Kremers WK, et al. Hyponatremia and mortality among patients on the liver-transplant waiting list. *N Engl J Med*. 2008;359:1018–1026.

Murray KF, Carithers RL Jr. AASLD practice guidelines: evaluation of the patient for liver transplantation. *Hepatology*. 2005;41:1407–1432.

A.5. Describe the cardiovascular system of patients with end-stage liver disease (ESLD).

The cardiovascular system of patients with ESLD mimics the hyperdynamic circulatory changes of patients with sepsis. Tachycardia, elevated cardiac output, low arterial blood pressure, and low systemic vascular resistance are characteristic. Enhanced endogenous production or diminished hepatic clearance of vasodilating substances, such as nitric oxide, carbon monoxide, and endogenous cannabinoids, and the inflammatory response to bacterial translocation cause splanchnic arterial vasodilation. Increased venous capacitance from formation of portosystemic shunts because of portal hypertension increases venous capacitance and contributes to a hyperdynamic circulation. Despite the frequent finding of a high cardiac output in patients with cirrhosis, echocardiography may reveal myocardial contractile impairment similar to that seen in sepsis. Patients with portal hypertension may develop portopulmonary hypertension and right ventricular dysfunction. A mean pulmonary artery pressure greater than 25 mm Hg at rest and a pulmonary vascular resistance greater than 240 dynes/s/cm^{-5} define portopulmonary hypertension.

Iwakiri Y, Groszmann RJ. The hyperdynamic circulation of chronic liver diseases: from the patient to the molecule. *Hepatology*. 2006;S121–S131.

Rodriguez-Roisin R, Krowka M, Hervé P, et al. Pulmonary-hepatic vascular disorders (PHD). *Eur Respir J*. 2004;24:861–880.

Steadman RH, Van Rensburg A, Kramer DJ. Transplantation for acute liver failure: perioperative management. *Curr Opin Organ Transplant*. 2010;15:368–373.

A.6. What causes acute kidney injury (AKI) in patients with cirrhosis?

Patients with AKI and cirrhosis have more complications and increased risk of mortality after liver transplantation than those without renal failure. Gastrointestinal bleeding, diarrhea from infection or lactulose administration, and diuretic medications change circulatory function via hypovolemia and can cause renal injury. As cirrhosis progresses, a reduction in systemic vascular resistance causes compensatory activation of the renin-angiotensin and sympathetic nervous systems, which leads to ascites, edema, and vasoconstriction of the intrarenal circulation and renal hypoperfusion.

Hepatorenal syndrome (HRS) is caused by functional renal vasoconstriction in response to splanchnic arterial vasodilation. Although histologic findings and diagnostic tests for HRS are lacking, diagnostic criteria are used to categorize two types of HRS. Criteria for HRS include (1) cirrhosis with ascites; (2) serum creatinine greater than 1.5 mg per dL; (3) no improvement of creatinine after 2 days of diuretic withdrawal and volume expansion with albumin; (4) absence of shock; (5) no current or recent treatment with nephrotoxic drugs; and (6) absence of parenchymal kidney disease. Type I HRS involves rapid and progressive impairment of renal function with a doubling of the initial serum creatinine to a level greater than 2.5 mg per dL or a 50% reduction in the 24-hour creatinine clearance to lower than 20 mL per minute in less than 2 weeks. Patients with type II HRS have impaired renal function and a serum creatinine greater than 1.5 mg per dL and do not meet the criteria for type I HRS. Compared with patients diagnosed with prerenal failure, patients with HRS lack a renal response to a 1.5 L volume challenge. Distinguishing between HRS and acute tubular necrosis is difficult. A fractional excretion of sodium less than 1% suggests tubular function and favors a diagnosis of HRS. The presence of renal tubular epithelial cells in urinary sediment favors a diagnosis of acute tubular necrosis.

Medical management of HRS is marginally effective, but liver transplantation usually reverses HRS. Kidneys transplanted from patients with HRS function normally in new hosts, suggesting the essential role of hepatic disease in the pathogenesis.

Gines P, Guevara M, Arroyo V, et al. Hepatorenal syndrome. *Lancet*. 2003: 362:1819–1827.

Gines P, Schrier RW. Renal failure in cirrhosis. *N Engl J Med*. 2009:361:1279–1290.

Meltzer J, Brentjens TE. Renal failure in patients with cirrhosis: hepatorenal syndrome and renal support strategies. *Curr Opin Anaesth*. 2010;23:139–144.

Salerno F, Gerbes A, Gines P, et al. Diagnosis, prevention and treatment of hepatorenal syndrome in cirrhosis. *Gut*. 2007;56:1310–1318.

A.7. What causes hyponatremia in patients with cirrhosis?

Patients with advanced cirrhosis have decreased effective blood volume and then circulatory dysfunction. They develop hypervolemic hyponatremia from increased secretion of antidiuretic hormone, which acts on the vasopressin-2 receptors of the renal tubular collecting duct to impair excretion of solute-free water. These patients have expanded extracellular volume, ascites, and edema.

Patients who develop hypovolemic hyponatermia via loss of extracellular fluid from the kidneys (overdiuresis) or gastrointestinal tract rarely have ascites or edema. These patients may have prerenal failure from low plasma volume and dehydration or hepatic encephalopathy from a rapid reduction in serum osmolality.

Gines P, Guevara M. Hyponatremia in cirrhosis. Pathogenesis, clinical significance, and management. *Hepatology*. 2008;48:1002–1010.

Keegan MT, Wright DR. Sodium, potassium, and glucose management in organ transplantation. *Curr Opin Organ Transplant*. 2010;15:383–389.

A.8. Discuss the neurologic manifestations of acute and chronic liver disease.

Hepatic encephalopathy is a neuropsychiatric complication of acute and chronic liver disease with features that range from mild confusion to cerebral edema with intracranial hypertension. Patients have disturbances in consciousness, cognitive abilities, behavior, neuromuscular function, concentration, reaction time, memory, and/or electroencephalogram readings. The pathogenesis of hepatic encephalopathy is not understood, but most theories implicate elevated levels of ammonia, a gut-derived neurotoxin, which is shunted to the systemic circulation from the portal system. Bacteria in the gut produce ammonia, which crosses the blood–brain barrier into astrocytes that detoxify it to glutamine. Astrocytes regulate neurotransmission, but their function is decreased when they swell because of increased concentrations of intracellular glutamine. High serum ammonia levels characterize patients with hepatic encephalopathy, even though the degree of elevation of ammonia does not correlate with neurologic severity. This observation suggests that other factors, such as hyponatremia, gastrointestinal bleeding, and infection contribute to the development of hepatic encephalopathy. Left untreated, cerebral edema can progress to intracranial hypertension and herniation of the brain.

Bernal W, Auzinger G, Dhawan A, et al. Acute liver failure. *Lancet*. 2010;376:190–201.

Gines P, Guevara M. Hyponatremia in cirrhosis. Pathogenesis, clinical significance, and management. *Hepatology*. 2008;48:1002–1010.

Teperman LW, Peyregne VP. Considerations on the impact of hepatic encephalopathy treatments in the pretransplant setting. *Transplantation*. 2010;89:771–778.

Zafirova Z, O'Connor M. Hepatic encephalopathy: current management strategies and treatment, including management and monitoring of cerebral edema and intracranial hypertension in fulminant hepatic failure. *Curr Opin Anaesthesiol*. 2010;23:121–127.

A.9. Why do patients with ESLD have abnormalities of hemostasis?

Patients with ESLD have hemostatic changes that promote both bleeding and thrombosis. Inadequate synthesis of all coagulation factors (except for von Willebrand factor), thrombocytopenia, platelet function defects, dysfibrinogenemia, and elevated tissue plasminogen activator (tPA) levels cause bleeding. Elevations of von Willebrand factor and factor VIII, and decreased levels of a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13 (ADAMTS-13), protein C, protein S, antithrombin, alpha 2-macroglobulin, plasminogen, and heparin cofactor II favor thrombosis. Thrombin generation is normal in cirrhosis, and in coagulation tests (prothrombin time [PT] and activated partial thromboplastin time [aPTT]), thrombin generation is considered a function of procoagulant factors and anticoagulant factors that inhibit thrombin are not considered.

Levels of fibrinogen, an acute phase reactant, are normal or increased in liver disease. Patients with severe hepatic dysfunction, however, may synthesize fibrinogen poorly, which increases the risk of bleeding. Although high concentrations of fibrinogen are found in patients with chronic hepatitis, cholestatic jaundice, and hepatocellular carcinoma, clot formation is not enhanced because fibrinogen is dysfunctional. Patients may have an abnormal thrombin time with normal PT and aPTT values.

Thromboyctopenia and platelet dysfunction are characteristic of ESLD. Thrombocytopenia results from several factors: hypersplenism, which sequesters

platelets; consumption of platelets during systemic intravascular coagulation; and impaired hepatic synthesis of thrombopoietin, which produces platelets in the bone marrow. Defective signal transduction; uremia from AKI; and intrinsic defects of adenosine diphosphate (ADP), arachidonic acid, collagen, and thrombin prevent platelet aggregation.

There may be little evidence of deranged coagulation when normal hepatic parenchyma is preserved, such as in an isolated hepatoma.

Dalmau A, Sabate A, Aparicio I. Hemostasis and coagulation monitoring and management during liver transplantation. *Curr Opin Organ Transplant*. 2009;14: 286–290.

Lisman T, Porte RJ. Rebalanced hemostasis in patients with liver disease: evidence and clinical consequences. *Blood*. 2010;116:878–885.

Senzolo M, Burra P, Cholongitas E, et al. New insights into the coagulopathy of liver disease and liver transplantation. *World J Gastroenterol*. 2006;12: 7725–7736.

A.10. What is the differential diagnosis for hypoxemia in patients with cirrhosis?

Potential causes of preoperative hypoxemia and respiratory failure in patients with cirrhosis includes atelectasis from the compressive effects of ascites, hepatic hydrothorax, hepatopulmonary syndrome (HPS), and underlying chronic pulmonary disease. Muscle wasting and intra-abdominal hypertension from ascites increase the work of breathing.

Ascites fluid can enter the pleural space through small channels in the diaphragm to cause a hepatic hydrothorax (usually on the right side). Negative intrathoracic pressure during inspiration facilitates movement of fluid from the peritoneum to the pleural space to minimize ascites.

A diagnosis of HPS is considered in patients without cardiopulmonary disease who have a Pao_2 less than 60 mm Hg. The triad of liver disease and/or portal hypertension, widened age-corrected alveolar-arterial oxygen gradient (more than 15 to 20 mm Hg) while breathing room air, and documented intrapulmonary vascular dilation (IPVD) define HPS. Enhanced production or impaired hepatic clearance of endogenous vasodilators (i.e., nitric oxide, vasodilator prostaglandins, substance P), or inhibition of vasconstrictive substances (i.e., tyrosine, serotonin, and endothelin) by a damaged liver may cause IPVD. IPVD causes hypoxemia via ventilation–perfusion mismatching, intrapulmonary shunt physiology, and diffusion limitation. Patients with HPS often complain of dyspnea and fatigue; they may have clubbing and spider angiomata on physical examination. Patients may experience platypnea (dyspnea in the upright position relieved by recumbency) or have orthodeoxia (arterial oxyhemoglobin desaturation in the upright position). Preferential perfusion of IPVD (while the patient is upright) may cause these clinical manifestations. Contrast-enhanced echocardiography detects intrapulmonary shunting suggestive of IPVD. Resolution of this syndrome after transplant has been reported.

Hemprich U, Papadakos PJ, Lachmann B. Respiratory failure and hypoxemia in the cirrhotic patient including hepatopulmonary syndrome. *Curr Opin Anaesthesiol*. 2009;23:133–138.

Rodriguez-Roisin R, Krowka MJ. Hepatopulmonary syndrome: a liver-induced lung vascular disorder. *N Engl J Med*. 2008;358:2378–2387.

A.11. What is portal hypertension? What are the sequelae of portal hypertension?

The normal portosystemic gradient between the portal vein and hepatic vein is less than 5 mm Hg. Intrahepatic vascular resistance and portal venous blood flow increase this gradient and characterize portal hypertension. Liver fibrosis, regenerative nodules, collagen deposition in the space of Disse, endothelial dysfunction, and an imbalance between endogenous vasoconstrictors (e.g., norepinephrine, thromboxane A, endothelin I, angiotensin II, leukotrienes) and vasodilators, such as nitric oxide, increase vascular resistance in the liver. As the pressure gradient between the portal vein and the hepatic vein increases, collaterals such as gastroesophageal and hemorrhoidal varices develop to decompress the portal system. Portal hypertension produces endogenous vasodilators that cause splanchnic vasodilation. Splanchnic vasodilation in turn increases portal blood flow and exacerbates portal hypertension.

Complications of portal hypertension include gastrointestinal bleeding from expansion and rupture of varices and intraoperative bleeding from intra-abdominal collaterals.

Dib N, Oberti F, Cales P. Current management of the complications of portal hypertension: variceal bleeding and ascites. *CMAJ.* 2006;174:1433–1443.

Garcia-Tsao G, Bosch J. Management of varices and variceal hemorrhage in cirrhosis. *N Engl J Med.* 2010;362:823–832.

B. Preoperative Evaluation and Preparation

B.1. What preoperative workup is desirable?

Anesthesiologists face several preoperative challenges when patients with ESLD disease need surgery. Surgical and anesthetic management is complicated for patients with an encephalopathy, AKI, electrolyte abnormalities, ascites, myocardial and pulmonary dysfunction, or coagulopathy. Physiologic perturbations during the perioperative period may precipitate multisystem organ failure. To anticipate and prevent complications from transplantation, underlying conditions should be thoroughly evaluated before surgery. A multidisciplinary team including an anesthesiologist, hepatologist, and surgeon should be involved in preoperative preparation. Consultations may be requested with cardiology, pulmonary, infectious diseases, and nephrology (especially if renal replacement therapy is considered) for patients with comorbidities.

Echocardiography is useful to detect cardiac dysfunction. The chest radiograph rules out pulmonary edema or cardiomegaly in patients with signs and symptoms of pulmonary edema or heart failure. Electrolyte levels, blood urea nitrogen, creatinine levels, albumin levels, bilirubin levels, complete blood count, coagulation parameters, and glucose values should be obtained. In cases of altered mental status, a head CT scan often is indicated to evaluate intracranial bleeding, herniation, and/or the extent of cerebral edema. Patients who may have received multiple previous transfusions, such as patients with a history of gastrointestinal bleeding, should be evaluated in advance for crossmatching large quantities of blood products for a transplant operation.

Patients of advanced age or those with risk factors may undergo cardiopulmonary testing for myocardial ischemia (e.g., dobutamine stress echocardiography), cardiac dysfunction (e.g., transthoracic echocardiography), or lung disease (e.g., pulmonary function tests).

Risk factors for adverse cardiac outcomes after liver transplantation include history of stroke, coronary artery disease, and increased intraventricular thickness.

Preoperative myocardial evaluation is recommended, typically with functional stress echocardiography and dobutamine. The heart rate must reach 85% of the maximum predicted heart rate for the stress test to be considered adequate. A vasodilatory (e.g., adenosine, persantine) myocardial stress test is less useful because in patients with ESLD, the resting vascular tone is so low that provoking vasodilation with drugs is impossible. Transthoracic echocardiography is useful to estimate right ventricular systolic pressure as a gauge of pulmonary artery pressure. If elevated, pretransplant right heart catheterization may be warranted.

If intraoperative renal replacement (continuous venovenous hemofiltration) therapy is a consideration, a nephrologist should be consulted.

Safadi A, Homsi M, Maskoun W, et al. Perioperative risk predictors of cardiac outcomes in patients undergoing liver transplantation surgery. *Circulation*. 2009;120:1189–1194.

Sandberg WS, Raines D. Anesthesia for liver surgery. In: Longnecker DE, Tinker JH, Morgan GE, eds. *Principles and Practice of Anesthesiology*. 3rd ed. St. Louis: Mosby; 2007.

Sharma P, Rakela J. Management of pre-liver transplant patients—part 1. *Liver Transpl*. 2005;11:124–133.

Sharma P, Rakela J. Management of pre-liver transplant patients—part 2. *Liver Transpl*. 2005;11:249–260.

Wiklund RA. Preoperative preparation of patients with advanced liver disease. *Crit Care Med*. 2004;32:S106–S115.

B.2. How is ascites managed preoperatively?

Ascites is initially managed with a low sodium diet and diuretic therapy. Patients with ascites refractory to treatment with diuretics may require large volume paracentesis and albumin replacement. Large-volume paracentesis is a risk factor for the development of HRS. Patients may be treated with a transjugular intrahepatic portosystemic shunt (TIPS) in refractory cases of ascites.

B.3. How is hyponatremia managed preoperatively?

Hyponatremia is associated with HRS, ascites, death from liver disease, and postoperative mortality after transplantation. Distinguishing between hypervolemic and hypovolemic hyponatremia guides treatment. Hypervolemic hyponatremia is managed with fluid restriction (1 to 1.5 L per day) and withholding of diuretics. Vaptans, medications that block the vasopressin-2 receptor, increase solute-free water excretion dose dependently and may preclude water restriction so that diuretics can be continued. Patients with hypovolemic hyponatremia are not given diuretics; instead saline is administered to increase plasma volume.

Patients who undergo orthotopic liver transplantation are at risk for central pontine myelinolysis (CPM) perioperatively. CPM is a neurologic condition characterized by symmetric noninflammatory demyelinating lesions in the basis pontis. The etiology of CPM is uncertain, but osmotic stress on central nervous system cells is theorized, and CPM correlates with rapid correction of hyponatremia. Rapid changes in concentration of serum sodium cannot be predicted and a "safe" rate of correction of hyponatremia has not been definitively established; some experts recommend sodium correction at a rate less than 12 mEq/L/day.

Preoperative correction of hyponatremia may prevent a rapid rise in serum sodium intraoperatively and postoperatively. During intraoperative fluid replacement, high sodium loads may cause rapid swings in serum sodium, or even hypernatremia, by the end of the case. Sodium bicarbonate should be administered cautiously because it has a high concentration of sodium.

Bernal W, Auzinger G, Dhawan A, et al. Acute liver failure. *Lancet*. 2010; 376:190–201.

Gines P, Guevara M. Hyponatremia in cirrhosis. Pathogenesis, clinical significance, and management. *Hepatology*. 2008;48:1002–1010.

Teperman LW, Peyregne VP. Considerations on the impact of hepatic encephalopathy treatments in the pretransplant setting. *Transplantation*. 2010;89:771–778.

Zafirova Z, O'Connor M. Hepatic encephalopathy: current management strategies and treatment, including management and monitoring of cerebral edema and intracranial hypertension in fulminant hepatic failure. *Curr Opin Anaesthesiol*. 2010;23:121–127.

B.4. What is a transjugular intrahepatic portosystemic shunt (TIPS) procedure? What is the role of TIPS in the management of patients with ESLD?

During a TIPS procedure, an expandable stent is placed into the liver parenchyma for portosystemic exchange and to decrease portal hypertension. This intervention may prevent recurrent variceal bleeding and manage refractory ascites. The procedure is performed under local or general anesthesia as a "bridge" to liver transplantation in patients with severe liver disease. Unlike older, surgically created portosystemic (e.g., splenorenal) and peritoneovenous (e.g., LeVeen shunt) shunts, a TIPS does not require abdominal operation or vascular diversion, both of which impose technical hazards to future liver transplantation.

Among the complications associated with the TIPS procedure are bleeding, infection, hemobilia, and stent migration. Encephalopathy may worsen from enhanced systemic delivery of biogenic amines normally cleared by the liver. The long-term patency of a TIPS is poor, and revisions may be needed before liver transplantation.

Boyer TD, Haskal ZJ. The role of transjugular intrahepatic portosystemic shunt in the management of portal hypertension (American Association for the Study of Liver Disease practice guideline). *Hepatology*. 2005;41:386–400.

Ochs A, Rossle M, Haag K, et al. The transjugular intrahepatic portosystemic stent-shunt procedure for refractory ascites. *N Engl J Med*. 1994;332:1192–1197.

Rossle M, Haag K, Ochs A, et al. The transjugular intrahepatic portosystemic stent-shunt procedure for variceal bleeding. *N Engl J Med*. 1994;330:165–171.

Scher C. Anesthesia for transjugular intrahepatic portosystemic shunt. *Int Anesthesiol Clin*. 2009;47:21–28.

Yonker-Sell AE, Connolly LA. Mortality during transjugular intrahepatic portosystemic shunt placement. *Anesthesiology*. 1996;84:231–233.

B.5. How are hepatic encephalopathy and elevated intracranial pressure (ICP) treated?

Initial therapy for hepatic encephalopathy identifies and treats reversible triggers (i.e., gastrointestinal bleeding and infection) of this neuropsychiatric syndrome. Nonabsorbable disaccharides such as lactulose decrease absorption of ammonia from the gut via catharsis. Excessive dosing of lactulose causes dehydration. Oral antibiotics (rifaximin, neomycin, vancomycin, paramomycin, or metronidazole) reduce ammonia-producing enteric bacteria. Rifaximin, in combination with lactulose, may prevent episodes of hepatic encephalopathy.

Patients who develop fulminant hepatic failure are at risk for hepatic encephalopathy, cerebral edema with increased ICP, and a threat of herniation. ICP monitoring should be seriously considered for patients with fulminant hepatic failure and encephalopathy, even given the bleeding risks associated with invasive monitors. Bleeding

risk seems to be the greatest deterrent to ICP monitoring. A review of recent data indicates a risk of approximately 10% for intracranial hemorrhage with insertion of a monitor. To minimize the risk, epidural transducers are recommended rather than intradural monitors. With or without ICP monitoring, 30-day outcomes are similar.

ICP elevations to greater than 25 mm Hg should be treated with mannitol to achieve hyperosmolarity. Preoperative hyperventilation has not been shown to improve outcome and corticosteroids are not indicated. Pentobarbital coma may be indicated for patients unresponsive to mannitol, but coma may worsen cerebral hypoperfusion by causing systemic hypotension. Many centers consider sustained cerebral hypoperfusion (cerebral perfusion pressure <40 mm Hg), a contraindication to transplant because of the high risk for brain death. In the future, transcranial Doppler ultrasonography may offer a noninvasive means of monitoring for elevated ICP in these patients. For anesthesia, drugs or conditions that exacerbate elevations in ICP should be avoided.

Bass NM, Mullen KD, Sanyal A, et al. Rifaximin treatment in hepatic encephalopathy. *N Eng J Med*. 2010;362:1071–1081.

Bernal W, Auzinger G, Dhawan A, et al. Acute liver failure. *Lancet*. 2010;376:190–201.

Gines P, Guevara M. Hyponatremia in cirrhosis. Pathogenesis, clinical significance, and management. *Hepatology*. 2008;48:1002–1010.

Teperman LW, Peyregne VP. Considerations on the impact of hepatic encephalopathy treatments in the pretransplant setting. *Transplantation*. 2010;89:771–778.

Zafirova Z, O'Connor M. Hepatic encephalopathy: current management strategies and treatment, including management and monitoring of cerebral edema and intracranial hypertension in fulminant hepatic failure. *Curr Opin Anaesthesiol*. 2010;23:121–127.

B.6. Should this patient be transfused with fresh frozen plasma prior to surgery?

Management of coagulopathy is challenging because blood tests such as PT and aPTT do not predict bleeding during liver transplantation.

Patients who need an orthotopic liver transplant usually have severe perturbations in coagulation, but it is neither necessary nor possible to correct them preoperatively. Patients with active sites of bleeding should be transfused with fresh frozen plasma, packed red blood cells, cryoprecipitate, or platelets as dictated by clinical assessment and laboratory tests. In addition, desmopressin (1-desamino-8-D-arginine vasopressin [DDAVP]) may be considered for patients with concomitant renal dysfunction and uremic bleeding. Potentially curative transplant surgery should not be postponed to correct coagulation defects.

C. Intraoperative Management

C.1. What monitors would you use? Why?

In addition to the monitors recommended by the American Society of Anesthesiologists (electrocardiogram, pulse oximetry, capnography, temperature, and noninvasive blood pressure), a radial arterial catheter is placed for beat to beat blood pressure monitoring and frequent sampling of blood. Pulse pressure variation, calculated from the invasive arterial tracing, assesses fluid responsiveness. A second arterial catheter is placed in the femoral artery to measure central aortic blood pressure. Peripheral arterial pressures may not be reliable in a patient with vasoconstriction, vasodilation, or compression of the subclavian artery with rib retraction.

Central line access is established to measure right atrial pressure and to administer drugs. Central venous pressure monitoring does not reliably measure blood volume or change in blood volume. The use of a pulmonary artery catheter depends on local practice and the physiologic state of the patient. Mixed venous oxygen saturation values are measured to assess cardiac output, but these measurements also are influenced by changes in oxygen-carrying capacity and oxygen consumption.

Transesophageal echocardiography (TEE) assesses ventricular filling, contractility, and function. Diagnoses such as myocardial ischemia, pulmonary embolism, pleural effusions, and inadequate inferior vena cava (IVC) reconstruction can be observed with TEE. The risk of rupture of esophageal varices with TEE is rare.

Krenn C, De Wolf, AM. Current approach to intraoperative monitoring in liver transplantation. *Curr Opin Organ Transplant*. 2008;13:285–290.

C.2. What are the considerations for the induction of anesthesia?

If there is evidence of tense ascites, recent food ingestion, or a propensity for delayed gastric emptying, a rapid-sequence induction of general endotracheal anesthesia is performed. AKI with elevated potassium levels or prolonged immobilization may preclude the use of succinylcholine. Compressive atelectasis from ascites and pleural effusions reduce functional residual capacity and decrease the time to oxygen desaturation. Vasodilating anesthetic agents may cause hypotension if intravascular volume is depleted (i.e., overdiuresis or gastrointestinal losses).

C.3. How does liver disease affect intraoperative medication management?

In patients with liver disease and edema, muscle relaxant doses are increased because fluid retention increases volume of distribution. The duration of action of muscle relaxants that are metabolized by the liver (i.e., vecuronium and rocuronium) is prolonged.

Many anesthetic drugs (i.e., opioids, barbiturates) bind to albumin in the circulation. Low albumin levels increase the free fraction of drug and can theoretically exaggerate the drug's clinical effect. ESLD, however, alters many other aspects of normal pharmacokinetics such as drug volume of distribution, hepatic extraction and metabolism, renal excretion, and levels of serum proteins other than albumin. The net effect of these changes is unpredictable, making general recommendations for drug administration difficult. A safe approach in these patients is to titrate the drug to the desired effect.

Patients with ESLD often exhibit coagulation disorders. The presence of a coagulopathy is a contraindication to regional anesthesia, particularly epidural anesthesia. Patients without an initial disorder of coagulation may develop a coagulopathy intraoperatively or postoperatively.

Wiklund RA. Preoperative preparation of patients with advanced liver disease. *Crit Care Med*. 2004;32:S106–S115.

C.4. What happens during the first stage (preanhepatic phase) of the liver transplant operation?

The preanhepatic phase begins with induction of anesthesia and ends with clamping of the hepatic artery. The diseased liver is mobilized; the suprahepatic and infrahepatic vena cava, portal vein, and hepatic artery are isolated; and the bile duct is divided. The anesthesia team manages disorders of coagulation and hemodynamic disturbances. Large losses of ascites cause hypotension and require early fluid resuscitation. Albumin solution and fresh frozen plasma are often used to replete intravascular volume.

C.5. What happens during the second stage (anhepatic phase) of the liver transplant operation?

The second stage of the liver transplant operation, the anhepatic phase, begins after removal of the diseased liver and ends with reperfusion of the new liver. If the IVC and portal vein are clamped, venous return to the heart and cardiac output decreases. In preparation for clamping and dividing the IVC, a test clamp maneuver (occlusion of the suprahepatic IVC) is performed to assess the resilience of the circulatory system. Hypotension is managed with vasoactive medications, fluid repletion, adjustment of anesthetic agents, correction of hypocalcemia, and venovenous bypass. Anastomoses between the recipient and donor liver are performed in the following order: caval, portal, hepatic artery, and biliary.

Polak WG, Peeters PM, Slooff MJ. The evolution of surgical techniques in clinical liver transplantation. A review. *Clin Transplant*. 2009:23:546–564.

C.6. What physiologic disturbances should be anticipated during the second stage (anhepatic phase) of the liver transplant operation?

Without a liver, the patient may develop acidosis and hypocalcemia because lactic acid and citrate are not cleared. Acidemia, reduced urine output, and the absence of hepatic uptake of potassium cause hyperkalemia. The liver regulates glucose levels, but in the anhepatic phase, gluconeogenesis is absent. Blood glucose levels are monitored for both hyperglycemia and hypoglycemia.

Merritt WT. Metabolism and liver transplantation: review of perioperative issues. *Liver Transpl*. 2000;6(4 suppl 1):S76–S84.

C.7. What is venovenous bypass? What are potential advantages and disadvantages of this procedure?

Some centers routinely use venovenous bypass to divert blood flow from the portal circulation and IVC to the right atrium. A Y-shaped tubing is used. One limb of the tubing is inserted into the recipient's portal vein to drain the splanchnic beds. Another limb of the tubing is placed, through a groin cut, down into an iliac vein or the distal IVC. The outflow tubing passes through a pump. Blood returns to the patient through a cutdown access to an axillary vein or through percutaneous access to an internal jugular or subclavian vein (Fig. 15.2).

Potentially, venovenous bypass can decompress the portal circulation and reduce congestion of the gut; decrease hemodynamic instability during clamping of the IVC; maintain normothermia via continuous warming of the bypass circuit; manage blood volume overload; preserve renal perfusion pressure; and improve surgical exposure during dissection. Disadvantages include the complications of venous cannula placement (bleeding, air, or thrombotic embolism); release of proinflammatory mediators; activation of complement, which may contribute to tissue injury and organ failure; and the time and cost of an expensive procedure.

The efficacy and benefits of routine use of venovenous bypass remain controversial. However, portal decompression clearly improves surgical visualization in certain circumstances, such as in Budd-Chiari syndrome. Other centers reserve venovenous bypass for situations in which interrupted venous return through the IVC depresses the recipient's circulating system.

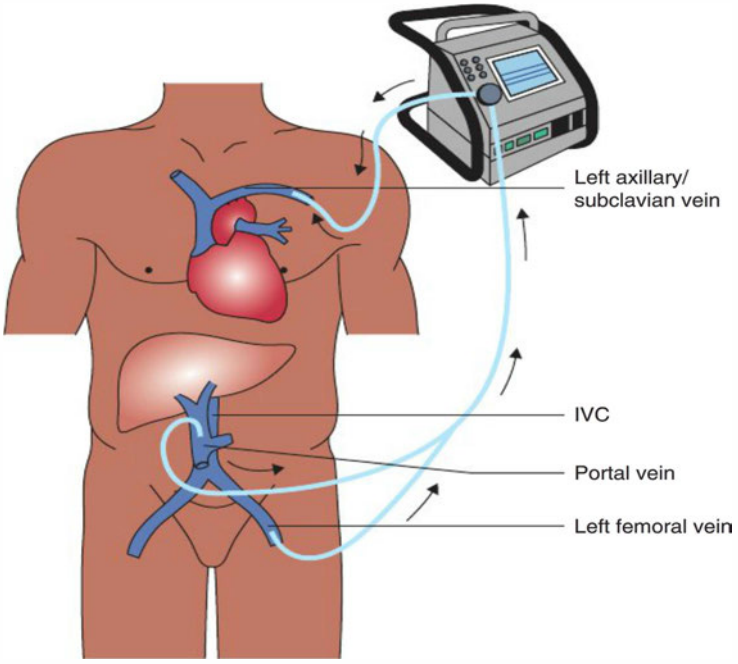

Figure 15.2 Schematic diagram of venovenous bypass circuit during liver transplantation. Venous return comes from the femoral and portal veins connected with the tubing connected together into a single venous return line. The centrifugal pump returns the blood into the axillary or subclavian vein. IVC, inferior vena cava.

Barnett R. Pro: Veno-veno bypass should routinely be used during liver transplantation. *J Cardiothorac Vasc Anesth.* 2006;20:742–743.

Hilmi IA, Planinsic R. Con: Venovenous bypass should not be used in orthotopic liver transplantation. *J Cardiothorac Vasc Anesth.* 2006;20:744–747.

Hoffmann K, Weigand MA, Hillebrand N, et al. Is veno-venous bypass still needed during liver transplantation? A review of the literature. *Clin Transplant.* 2009;23:1–8.

Polak WG, Peeters PM, Slooff MJ. The evolution of surgical techniques in clinical liver transplantation. A review. *Clin Transplant.* 2009:23:546–564.

C.8. What surgical techniques anastomose the donor and recipient inferior vena cava?

There are several techniques to anastomose the donor and recipient IVC. Conventionally, blood flow through the IVC is completely interrupted and a cylinder of the recipient's IVC is removed with the diseased liver. An end-to-end anatomosis is created between the donor's and the recipient's IVC (Fig. 15.3A). In the piggyback method, the diseased liver is dissected off the IVC. The recipient's IVC is preserved and blood flow is not completely interrupted. One end of the graft's segment of IVC is oversewn, and the orifice of the hepatic veins (the liver's venous outflow) is anastomosed to the preserved recipient's suprahepatic IVC (Fig. 15.3B). A third technique creates a side-to-side cavo-caval anastomosis (Fig. 15.3C).

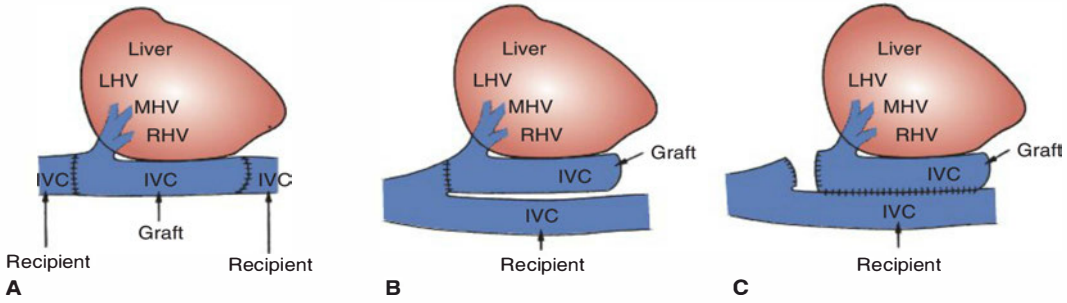

Figure 15.3 Three different techniques to reconstruct the hepatovenous outflow. **A.** End-to-end interposition of the donor vena cava to the recipient vena cava. **B.** End-to-end anastomosis of the vena cava to the hepatic veins. **C.** Side-to-side cavo-cavostomy. (Reproduced and modified with permission from Hesse UJ, Berrevoet F, Troisi R, et al. Hepato-venous reconstruction in orthotopic liver transplantation with preservation of the recipients' inferior vena cava and veno-venous bypass. *Langenbecks Arch Surg.* 2000;385:350–356.)

Mehrabi A, Fonouni H, Muller SA, et al. Current concepts in transplant surgery: liver transplantation today. *Langenbecks Arch Surg.* 2008;393:245–260.

Polak WG, Peeters PM, Slooff MJ. The evolution of surgical techniques in clinical liver transplantation. A review. *Clin Transplant.* 2009:23:546–564.

C.9. What are the potential advantages of the "piggyback" (vena cava preservation) technique?

Potential advantages of the piggyback technique for vascular reconstruction include hemodynamic stability because cardiac filling is preserved; protected perfusion pressure; nonneed for the surgical interventions associated with venovenous bypass; reduced need for retrocaval dissection, which lessens the likelihood of damage to the adrenal vein; and shorter anhepatic time and warm ischemia time. A disadvantage of the technique is that outflow obstruction results in hepatic congestion. Unfavorable anatomy in the recipient may preclude the the piggyback technique.

Polak WG, Peeters PM, Slooff MJ. The evolution of surgical techniques in clinical liver transplantation. A review. *Clin Transplant.* 2009:23:546–564.

C.10. What hemodynamic changes are expected after removal of vascular clamps? What is postreperfusion syndrome?

Removal of the suprahepatic IVC clamp is not associated with hemodynamic changes. Unclamping the infrahepatic IVC restores venous return.

After unclamping of the portal vein, desaturated blood from the obstructed portal circulation, inflammatory mediators such as Il-6 and TNF alpha, potassium, protons, and cold components are released into the systemic circulation. Hemodynamic instability, characterized by a decrease in blood pressure, heart rate, systemic vascular resistance, cardiac output, and an increase in pulmonary arterial

pressures, may follow unclamping of the portal vein and reperfusion of the liver. Careful flushing of the graft just before completion of the anastomoses attenuates reperfusion disturbances by removing the cold hyperkalemic preservative solution. A sustained 30% decrease in mean arterial blood pressure for more than 1 minute during the first 5 minutes after reperfusion defines postreperfusion syndrome. A prolonged cold ischemic time and the absence of portocaval shunting are associated with the development of postreperfusion syndrome. Before reperfusing the new graft, the following measures should be considered: (1) preemptive administration of calcium to correct hypocalcemia; (2) sodium bicarbonate, dichloroacetate, or tris-hydroxymethyl aminomethane to adjust pH; and (3) inotropes or vasopressors for circulatory support. The surgical and anesthesia teams must be prepared to diagnose and treat dysrhythmias or cardiac arrest.

Paugam-Burtz C, Kavafyan J, Merckx P, et al. Postreperfusion syndrome during liver transplantation for cirrhosis: outcome and predictors. *Liver Transpl.* 2009;15:522–529.

C.11. How would you treat hyperkalemia?

Hyperkalemia is treated with diuretics, β-adrenergic agonists, insulin in combination with glucose, and alkalinization via administration of sodium bicarbonate or hyperventilation. Dysrhythmic effects of elevated potassium may be countered with calcium. Rarely, when hyperkalemia is refractory to the preceding treatments, continuous venovenous hemofiltration may reduce the elevated serum potassium level.

Xia VW, Ghobrial RM, Du B, et al. Predictors of hyperkalemia in the prereperfusion, early postreperfusion, and late postreperfusion periods during adult liver transplantation. *Anesth Analg.* 2007;105:780–785.

C.12. Why should you anticipate hypocalcemia?

The principal reason to anticipate hypocalcemia is a failure to clear citrate, which normally is metabolized by the liver. This calcium-chelating agent accumulates in patients who receive transfusions of citrated blood products.

C.13. What happens during the third stage of the liver transplant operation?

The third stage of the liver transplant operation, the neohepatic phase, follows reperfusion of the new liver. In the neohepatic phase, the biliary drainage system is constructed. Reconstruction may be straightforward, with an anastomosis between the graft's common bile duct and the biliary stump of the recipient. More complex reconstructions are sometimes required, such as the creation of a choledochojejunostomy. A donor cholecystectomy generally is performed. A T-tube is placed in the reconstructed biliary outflow system, with external drainage. An intraoperative cholangiogram, with contrast dye instilled through the T-tube, is used to assess the patency and integrity of the biliary reconstruction. The third stage ends with closure of all wounds and transport to the intensive care unit.

During the third stage of the procedure, an insidious coagulopathy may develop, requiring transfusion.

Polak WG, Peeters PM, Slooff MJ. The evolution of surgical techniques in clinical liver transplantation. A review. *Clin Transplant.* 2009:23:546–564.

C.14. What causes intraoperative bleeding during each phase of liver transplantation? How is coagulopathy monitored and treated? What is thromboelastography (TEG)?

The etiology of intraoperative bleeding during liver transplantation is multifactorial. Patients with ESLD have serious hemostatic defects, and coagulation is affected by alterations in body temperature, tissue perfusion, acid–base balance, and fluid balance.

During the preanhepatic phase, bleeding from the surgical technique is influenced by the patient's underlying coagulopathy. Excessive fluid administration may cause a dilutional coagulopathy and increase venous congestion of the splanchnic area, leading to more bleeding at the surgical site. Bleeding may be minimal in a hypercoagulable state such as hepatocellular carcinoma or cholestatic cirrhosis.

During the anhepatic phase, there is a net increase in systemic tPA derived from endothelial cells, which is normally cleared by the liver. Although PT and aPTT values may not change, hyperfibrinolysis is possible. Hyperfibrinolysis is confirmed by a decrease in alpha-2-antiplasmin and plasminogen activity and an increase in fibrin and fibrinogen degradation products.

Nonsurgical and insidious bleeding during reperfusion can be profound. Disseminated intravascular coagulation, increased fibrinolysis, release of heparin or heparin-like substances, and trapped platelets in the graft cause coagulopathy.

The coagulation status should always be monitored by inspection of the surgical field. Routine laboratory tests (PT, aPTT, platelet count, fibrinogen levels) are used in some centers for evaluating the coagulation status and directing treatment. Other centers use TEG, a test of whole blood clotting function, to diagnose disorders of coagulation. TEG assesses the viscoelastic properties of a whole blood sample as a function of time. TEG detects a hypercoagulable state, and distinguishes hyperfibrinolysis from other causes of coagulopathy, such as factor depletion or thrombocytopenia (also see Chapter 11, section A.22). Heparinase may be used to help diagnose coagulopathy resulting from the presence of heparinoids.

Dalmau A, Sabate A, Aparicio I. Hemostasis and coagulation monitoring and management during liver transplantation. *Curr Opin Organ Transplant.* 2009;14:286–290.

Lisman T, Porte RJ. Rebalanced hemostasis in patients with liver disease: evidence and clinical consequences. *Blood.* 2010;116:878–885.

Senzolo M, Burra P, Cholongitas E, et al. New insights into the coagulopathy of liver disease and liver transplantation. *World J Gastroenterol.* 2006;12:7725–7736.

C.15. What are the complications of massive transfusion?

Uncontrolled hemorrhage and massive transfusion may cause the lethal triad of acidosis, coagulopathy, and hypothermia. Left uncorrected, each of these abnormalities can exacerbate the other, creating a "blood vicious cycle." Additional early complications of massive transfusion include (1) acute hemolytic transfusion reactions, (2) febrile nonhemolytic transfusion reactions, (3) transfusion-related acute lung injury, (4) transfusion-associated circulatory overload, (5) allergic reactions, (6) bacterial sepsis, (7) hypocalcemia, and (8) hyperkalemia.

Sihler KC, Napolitano L. Complications of massive transfusion. *Chest.* 2010;137:209–220.

C.16. How are the complications of massive transfusion prevented?

Warming the room, applying forced warming systems on the patient's body, administering blood products and fluids through a fluid warmer, and heating and humidifying inspired gases reduce the risk of hypothermia. Dilutional coagulopathy and thrombocytopenia may be prevented by transfusing packed red blood cells, fresh frozen plasma, and platelets in a 1:1:1 ratio. Occasionally, recombinant factor VIIa is administered. Potasssium, magnesium, and calcium levels are frequently monitored to correct abnormal levels. Metabolic acidosis is managed by improving hemodynamic parameters, adjusting minute ventilation, and administering sodium bicarbonate or tromethamine for severe metabolic acidosis. The risk of transfusion-related acute lung injury may be reduced by minimizing transfusions and transfusing packed red blood cells with a short storage time and fresh frozen plasma from men or nulliparous women.

Sihler KC, Napolitano L. Complications of massive transfusion. *Chest*. 2010;137:209–220.

C.17. How is hyperfibrinolysis managed?

tPA has been implicated as a causal agent in hyperfibrinolysis. A functioning graft liver will eventually clear excess tPA from the circulation. Pharmacologic therapy with antifibrinolytic agents (tranexamic acid, ε-aminocaproic acid [Amicar] or aprotinin [Trasylol]) blocks fibrin degradation by plasmin, but the full spectrum of their actions remains incompletely defined. The use of prophylactic antifibrinolytic agents in liver transplant surgery has been advocated, but this use is controversial. Potential disadvantages of antifibrinolytic agents include development of thromboses that may be catastrophic.

Groenland THN, Porte RJ. Antifibrinolytics in liver transplantation. *Int Anesthesiol Clin*. 2006;44:83–97.

Xia VW, Steadman RH. Antifibrinolytics in orthotopic liver transplantation: current status and controversies. *Liver Transpl*. 2005;11:10–18.

C.18. When is intraoperative renal replacement therapy indicated?

Managing patients with low urine output, renal dysfunction, or preoperative hyperkalemia who undergo liver transplantation is challenging. Continuous renal replacement therapy may be used intraoperatively to manage volume shifts, acid–base balance, and electrolyte disturbances. Patients who are receiving dialysis and patients who have AKI should have intraoperative continuous renal replacement therapy.

Townsend DR, Bagshaw SM, Gobney RT, et al. Intraoperative renal support during liver transplantation. *Liver Transpl*. 2009;15:73–78.

C.19. What intraoperative signs suggest that the hepatic graft is working?

Good texture and color of the graft, evidence of bile production, and hemodynamic stability are signs that the graft is working. Hypocalcemia often resolves quickly as the graft metabolizes citrate during the final phases of the procedure. Metabolic alkalemia can develop as a result of citrate metabolism. Potassium levels tend to normalize with the onset of hepatocyte function. A number of recipients exhibit hyperglycemia resistant to insulin.

D. Postoperative Management

D.1. What are the goals of immediate postoperative care of the liver transplant patient?

After liver transplantation, patients are admitted to the intensive care unit for monitoring of organ function, management of intraoperative complications, correction of coagulopathy, evaluation of graft function, and initiation of immunosuppression. Although many patients are extubated within 6 hours after the operation, the lungs of liver transplant patients often are mechanically ventilated for 24 to 48 hours.

D.2. What postoperative findings suggest that the hepatic graft is functioning?

Clearance of lactic acid, production of glucose, resolution of encephalopathy, normothermia, normalization of coagulopathy, decreasing total bilirubin levels, production of bile (through the biliary tube), and adequate urine output suggest a functioning graft. Preservation injury causes transaminases to rise immediately after surgery, but enzyme levels usually fall within 24 to 48 hours. New synthesis of coagulation factors will not correct factor depletion for hours to days after the transplant.

D.3. What coagulation disturbances should be anticipated in the postoperative period?

Typically, heparin effects, disseminated intravascular coagulation, or hyperfibrinolysis have been resolved in the operating room. However, dilutional coagulopathy, along with ongoing platelet and factor consumption in the early postoperative phase and poor graft function, may contribute to clinical bleeding. Postoperative uremia compromises platelet function. A functioning graft liver may not produce substantial levels of clotting factors for several days. Therefore, plasma, cryoprecipitate, and/or platelets may be needed in the early postoperative period.

D.4. Can renal function change after liver transplantation?

Postoperative renal function is correlated with preoperative glomerular filtration rate, and approximately 10% of liver transplant patients require postoperative dialysis. For patients with cirrhosis who have HRS resistant to diuretics, renal function may improve after transplantation. Postoperatively, sepsis and the nephrotoxic calcineurin inhibitors such as cyclosporin A and FK-506 (tacrolimus) may contribute to renal dysfunction. Balanced immunosuppression with steroids, mycophenolate mofetil, anti-CD25 (basiliximab/daclizumab) and antithymoglobulin can minimize posttransplant renal dysfunction. Chronic allograft nephropathy in patients who have received liver, heart, lung, or kidney transplants is now the third most common reason for patients to be on the waiting list for a kidney transplant.

Gines P, Schrier RW. Renal failure in cirrhosis. *N Engl J Med.* 2009:361:1279–1290.

D.5. What vascular and biliary complications occur after liver transplantation?

Arterial and venous vascular complications include anastomotic bleeding leading to hypovolemia and acute stenosis or occlusion from thrombosis or kinking of the graft vessels. Thrombosis of the portal vein or hepatic artery compromises viability of the graft. Abdominal Doppler ultrasound is used to assess the hepatic vessels. Hepatic artery thrombosis, which is more common than portal vein thrombosis, may cause severe liver failure from necrosis. Portal vein thrombosis may cause liver dysfunction, tense ascites, and variceal bleeding.

Patients with bile leaks experience fever, abdominal pain, and peritoneal irritation. Bile leaks develop early in the postoperative course and may be identified by ultrasonography showing abdominal fluid collections or cholangiography. Bile leaks are managed with endoscopic placement of a biliary stent or relaparotomy.

Mehrabi A, Fonouni H, Muller SA, et al. Current concepts in transplant surgery: liver transplantation today. *Langenbecks Arch Surg.* 2008;393:245–260.

D.6. What immunosuppressive agents will be given after liver transplantation? What are the major side effects?

The risk of organ rejection is balanced against the risk of medication toxicity. Protocols vary from center to center. A usual regimen includes cyclosporine or FK-506 (tacrolimus), azathioprine or mycophenolate mofetil, and prednisone. Antibodies directed against T-cell lymphocytes (e.g., OKT3 or antithymocyte globulin) may be substituted for cyclosporine or tacrolimus in patients with renal dysfunction or used in short courses to treat rejection. New drugs for immunosuppression in liver transplantation are monoclonal antibodies to IL-2 receptors (CD25) of T lymphocytes (basiliximab and daclizumab). The adverse effects of these medications are listed in Table 15.1.

Table 15.1 Adverse Effects of Immunosuppressant Medications

MEDICATION	ADVERSE EFFECTS
Cyclosporine	Nephrotoxicity Hypertension
FK-506 (tacrolimus)	Nephrotoxicity Hypertension
Mycophenolate mofetil	Hypertension Leukopenia Abdominal pain Diarrhea Vomiting
Azathioprine	Leukopenia Anemia Thrombocytopenia
Prednisone	Glucose intolerance Osteoporosis Peptic ulcer disease Adrenal suppression
OKT3	Symptoms of cytokine release (fever, chills, dyspnea, wheezing, chest pain) Leukopenia
Antithymocyte globulin	Fever Chills Leukopenia Thrombocytopenia
Basiliximab	Gastrointestinal upset
Daclizumab	Gastrointestinal upset

Feng SF, Ko DSC, Cosimi AB. Liver transplantation. In: Morris PJ, Wood WC, eds. *Oxford Textbook of Surgery*. 2nd ed. New York: Oxford University Press; 2000:685–707.

Moser MAJ. Options for induction immunosuppression in liver transplant recipients. *Drugs*. 2002;62:995–1011.

Yost CS, Niemann CU. Anesthesia for abdominal organ transplantation. In: Miller RD, ed. *Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone Elsevier; 2010:2155–2184.

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SECTION IV

The Nervous System

CHAPTER 16

Brain Tumor and Craniotomy

Kane O. Pryor and Hugh C. Hemmings, Jr.

A 47-YEAR-OLD WOMAN

who was previously healthy presents with a 4-month history of headache, with intermittent diplopia and gait disturbance developing over the last month. She is admitted after her husband witnesses an acute episode of profound lethargy, altered cognition, and vomiting. Neurologic examination is remarkable for abnormal right-sided cranial nerve V, VII, and VIII function, nystagmus, and ataxic gait. Magnetic resonance imaging (MRI) shows a large, right posterior fossa mass that is only slightly hyperintense on T2-weighted images, but is clearly demarcated after the intravenous injection of gadolinium contrast. The impression is of a petroclival meningioma, with mass effect on the pons and fourth ventricle. Magnetic resonance angiogram shows a highly vascular tumor drawing principal blood supply from the ascending pharyngeal branch of the ipsilateral external carotid artery. The patient improves clinically following the administration of dexamethasone and mannitol, and the infusion of 2% sodium chloride and is monitored in the neurosurgical intensive care unit (ICU). The day after admission, the patient undergoes uneventful cerebral angiography and partial embolization of the tumor under general anesthesia. She is now scheduled for posterior fossa craniotomy and resection of the tumor.

A. Medical Disease and Differential Diagnosis

1. What are the determinants of intracranial pressure (ICP)?
2. How does the presence of a mass alter the ICP in this patient?
3. What are the determinants of cerebral blood flow (CBF), and how are they altered by the presence of an intracranial tumor?
4. Are there any issues specific to posterior cranial fossa pathology?
5. What are the cerebral steal syndromes?
6. What is the role of preoperative embolization therapy?

B. Preoperative Evaluation and Preparation

1. What are special considerations in the preoperative evaluation of the patient scheduled for posterior fossa craniotomy?
2. In a patient who presents with intracranial hypertension, what management may have already been initiated preoperatively and what are the implications for anesthetic management?
3. How will intraoperative electromyography (EMG), sensory evoked potential (SEP), or brainstem auditory evoked response (BAER) monitoring affect the anesthetic management plan?
4. What are the options for patient positioning during posterior fossa surgery?
5. What are the principal disadvantages associated with the common posterior fossa craniotomy positions?
6. How should the patient position ultimately be determined?
7. How does the sitting position affect your preoperative assessment and planning?
8. Should this patient receive premedication?

C. Intraoperative Management

1. What are the anesthetic goals for craniotomy?
2. What monitors should be used during craniotomy?
3. What specific risks are associated with induction of anesthesia?
4. How would you induce anesthesia?
5. What are the effects of anesthetics on cerebral metabolic rate of oxygen ($CMRo_2$), CBF, and ICP? With this in mind, how would you maintain anesthesia?
6. How would you manage ventilation and maintain arterial carbon dioxide?
7. How would you approach diuretic therapy?
8. How would you manage serum glucose?
9. How would you approach fluid management?
10. Once the bone plate is removed and the dura retracted, the surgeon reports that the brain is still "tight." What would be your response?
11. If deliberate hypotension is indicated, how will you achieve it?
12. While the surgeon is resecting tumor from near the brainstem, the patient's heart rate suddenly drops to 20 beats per minute. What is your assessment and management?
13. Would you monitor for venous air embolism? What are the monitoring options?
14. Are there any measures you can take to prevent venous air embolism?
15. During the procedure, the precordial Doppler becomes loud and turbulent. The end-tidal CO_2 ($ETco_2$) drops from 31 mm Hg to 13 mm Hg, and the systemic blood pressure from 121/63 mm Hg to 64/32 mm Hg. What is your assessment and management plan?
16. What is your approach to emergence? What if the patient does not wake up?

D. Postoperative Management

1. What postoperative complications are of greatest concern? What level of monitoring is required?

A. Medical Disease and Differential Diagnosis

A.1. What are the determinants of intracranial pressure (ICP)?

The intracranial cavity is a rigid structure with minimal compliance. The structures within this cavity can be conceived of as belonging to one of three compartments:

- The *parenchymal compartment*, which is composed of two subcomponents—
  - a cellular component, which consists of the normal neuronal and glial cellular material, but also includes abnormal cellular volume from tumors;
  - a fluid component, which consists of the intracellular and extracellular fluid—capable of significant dynamic changes as a result of inflammatory responses and osmolarity gradients
- The *cerebrospinal fluid (CSF) compartment*
- The *blood compartment*, consisting of the arterial and venous subcompartments

If the volume of any one of these compartments increases, there is limited compensatory potential, especially if the expansion is rapid. Initially, CSF can drain to the spinal CSF reservoir and venous blood to the extracranial veins. Therefore, during the early phase of intracranial volume expansion, only a minimal increase in ICP may occur. At a critical point, these compensatory mechanisms are exhausted, and even small increases in intracranial volumes will result in significant increases in ICP. Because diminished intracranial compliance reserve can be clinically silent up to this point, review of MRI or computed tomography (CT) of the brain is critically important. As ICP increases, sedation, cognitive slowing, and nausea are likely to be early signs. Further increases in ICP can eventually lead to herniation of brain tissue through a noncompliant space—rapidly resulting in irreversible injury and often death.

Normal ICP is 5 to 15 mm Hg. Normal adult brain tissue volume is approximately 1400 mL, intracranial CSF volume is 75 to 100 mL, and cerebral vascular volume is approximately 150 mL.

Ursino M, Lodi CA. A simple mathematical model of the interaction between intracranial pressure and cerebral hemodynamics. *J Appl Physiol.* 1997;82:1256–1269.

A.2. How does the presence of a mass alter the ICP in this patient?

As the intracranial cavity is essentially of fixed volume, the volume of any intracranial mass must be accommodated by reduction in the volume of other intracranial contents, as described earlier. However, because the structures within the intracranial cavity are highly organized, the three-compartment model is overly simplistic. Thus, the neurologic sequelae of a mass, including effects on ICP, will vary significantly with its anatomic location and rapidity of growth. Elevated ICP is most often the result of direct space-occupying effects, resulting from both the tumor mass and surrounding edema. Thus, slow-growing tumors, such as meningiomas, can become astoundingly large without causing substantial increases in ICP as volume remodeling occurs; this is especially true of supratentorial hemispheric tumors. In contrast, even small masses in the posterior fossa can cause a noncommunicating hydrocephalus and elevated ICP by obstructing CSF outflow at the fourth ventricle. It is important to remember that

although compensatory mechanisms can maintain a normal or near-normal ICP, the patient with an intracranial mass will always have diminished reserve to accommodate increases in the volume of other intracranial contents.

In this patient, a slow-growing meningioma has been able to attain a large size before becoming symptomatic. The patient's earliest signs and symptoms were most likely due to a localized mass effect. Nevertheless, the acute decompensation, with rapidly developing signs and symptoms of elevated ICP, probably represent the added component of CSF outflow obstruction at the fourth ventricle. Even with the clinical improvement provided by steroid therapy and osmotic diuresis, this patient certainly has very little volume reserve and intracranial compliance even small further increases in volume—such as an increase in cerebral blood volume (CBV) precipitated by a minimum alveolar concentration (MAC) of volatile anesthetic—have the potential to cause a precipitous spike in ICP.

Ropper AH. Lateral displacement of the brain and level of consciousness in patients with an acute hemispheral mass. *N Engl J Med.* 1986;314:953–958.

Schaller B, Graf R. Different compartments of intracranial pressure and its relationship to cerebral blood flow. *J Trauma.* 2005;59:1521–1531.

A.3. What are the determinants of cerebral blood flow (CBF), and how are they altered by the presence of an intracranial tumor?

The brain receives a disproportionate percentage of cardiac output because of its high metabolic requirement (~3.5 mL O_2/min/100 g brain tissue). CBF flow is coupled to $CMRO_2$. At a wide range of mean arterial pressures (MAPs), the cerebral circulation alters its resistance to maintain a constant CBF—a process known as *autoregulation*. It has classically been taught that in the otherwise healthy brain, autoregulation maintains a relatively constant CBF between MAPs of approximately 50 and 150 mm Hg; above and below these values, CBF is pressure dependent. Based on recent studies in humans, the extremes of this range should be approached with caution, especially the lower boundary; CBF can decrease at MAPs of 60 or even 70 mm Hg. Special caution is required in patients with chronic systemic hypertension, in whom autoregulation right-shifts to accommodate the higher MAPs. Without active blood pressure support, many of these patients are at risk for extended periods during surgery at pressures below their autoregulation threshold.

CBF also varies with changes in $Paco_2$ between values of approximately 25 and 100 mm Hg. Increasing the partial pressure of carbon dioxide ($Paco_2$) from 40 to 80 mm Hg will roughly double CBF, and decreasing from 40 to 20 mm Hg will halve CBF. Importantly, the presence of hypercapnia decreases pressure-dependent autoregulation.

The presence of an intracranial mass can cause localized regions of high tissue pressure gradients, inflammation, and ischemia. These all contribute to dysfunction of normal autoregulation such that, in the brain regions surrounding the mass, regional CBF becomes pressure dependent over a greater range of pressures than in normal tissue. Further, if ICP becomes elevated above the level of the central venous pressure (CVP), the cerebral perfusion pressure (CPP = MAP − the greater of ICP or CVP) decreases. The ability of autoregulation to compensate for decreases in CPP is limited; therefore, if ICP is elevated, CBF can be low even in the presence of normally adequate MAPs. A conservative approach to management of CPP would suggest that it should not be allowed to fall below 70 mm Hg for any extended period in the baseline normotensive patient. Although a more moderate approach targeting CPPs in the 60- to 70-mm Hg range is commonly used, most neuroanesthesiologists agree that sustained CPP values under 60 mm Hg place the brain at risk, despite the possible neuroprotection afforded by the presence of a GABAergic anesthetic agent.

Giulioni M, Ursino M. Impact of cerebral perfusion pressure and autoregulation on intracranial dynamics: a modeling study. *Neurosurgery*. 1996;39:1005–1014.

Sharma D, Bithal PK, Dash HH et al. Cerebral autoregulation and CO_2 reactivity before and after elective supratentorial tumor resection. *J Neurosurg Anesthesiol*. 2010;22:132–137.

A.4. Are there any issues specific to posterior cranial fossa pathology?

Surgery for tumors in the posterior fossa presents several challenges not seen with supratentorial surgery. The posterior fossa is a tightly enclosed space in which tumors are often in direct contact with critical brainstem structures, including the cranial nerves and brainstem nuclei. The margin for error when operating near these structures is extremely small, as can be the spatial reserve for postoperative inflammation. The patient with a posterior fossa tumor, especially one close to the brainstem, can worsen neurologically in the hours following surgery as a result of postsurgical inflammation causing edema. This possibility must be considered when determining the appropriateness of extubation and postoperative management. Even with a successful resection and apparently adequate hemostasis, it might be appropriate to leave the patient intubated in anticipation of neurologic compromise as edema develops around the resected tumor bed.

In addition to the risk of neuronal damage, surgery in proximity to brainstem nuclei can trigger significant intraoperative autonomic and collateral hemodynamic instability, which can be extremely challenging to manage. The most common autonomic event is an acute increase in vagal tone, which in some instances can lead to a prolonged period of asystole, and can be immediately followed by a reflexive surge in sympathetic tone. Further, the risk to cranial nerves and other structures often demands intraoperative neurophysiologic monitoring—such as SEPs, brainstem auditory evoked potentials, or EMG—all of which can substantially restrict and dictate anesthetic management.

Finally, the posterior fossa cannot be accessed with the patient in the conventional supine position. In the past, the sitting position was highly favored by neurosurgeons and presented marked anesthetic challenges because of the increased risk of venous air embolism. Although still common in some centers, the sitting position has fallen out of favor; nonetheless, all of the positions that permit access to the posterior fossa pose management difficulties that must be considered. The risk of venous air embolism, although reduced, often still exists. Other considerations include loss of jugular outflow, deterioration of pulmonary compliance, strain on the cervical spine and brachial plexus, and a lack of access to central venous lines and the airway. In patients who are critically ill or otherwise at risk for life-threatening intraoperative events, it must be remembered that cardiopulmonary resuscitation will always require that the patient be rapidly returned to the supine position.

Bullock MR, Chesnut R, Ghajar J, et al. Surgical management of posterior fossa mass lesions. *Neurosurgery*. 2006;58:S47–S55.

Drummond JC, Todd MM. Acute sinus arrhythmia during surgery in the fourth ventricle: an indicator of brainstem irritation. *Anesthesiology*. 1984;60:232–235.

Gurol ME, St Louis EK. Treatment of cerebellar masses. *Curr Treat Options Neurol*. 2008;10:138–150.

Kan P, Couldwell WT. Posterior fossa brain tumors and arterial hypertension. *Neurosurg Rev*. 2006;29:265–269.

A.5. What are the cerebral steal syndromes?

Any intracranial pathology, including marginal ischemia and inflammation surrounding a mass lesion, can cause localized dysfunction of normal cerebral autoregulation and response to vasoactive agents. The microvasculature in the pathologic region can have an essentially fixed resistance. In this case, if vasodilation occurs in other normal regions of the brain, the decreased vascular resistance in the normal tissue can theoretically shunt blood flow away from the pathologic regions, which are already most vulnerable. This phenomenon is known as *cerebral steal*. In anesthesia management, cerebral steal is most relevant in the context of hypercapnia and the use of high concentrations (greater than 1 MAC) of volatile anesthetics. Both of these cause vasodilation of normal vasculature and potentially cause decreased regional CBF in pathologic areas. During hypocapnia, when there is vasoconstriction in normal tissue, the opposite may occur. In this case, blood flow to pathologic regions can actually increase. This phenomenon is known as *inverse steal* or the *Robin Hood effect*. Although there is a sound basis in the animal literature, the clinical relevance of steal and inverse steal phenomena in human patients has never been established. Nonetheless, it is prudent to consider it in anesthetic management.

Artru AA, Merriman HG. Hypocapnia added to hypertension to reverse EEG changes during carotid endarterectomy. *Anesthesiology*. 1989;70:1016–1018.

Darby JM, Yonas H, Marion DW, et al. Local "inverse steal" induced by hyperventilation in head injury. *Neurosurgery*. 1988;23:84–88.

Sato K, Shirane R, Kato M, et al. Effect of inhalational anesthesia on cerebral circulation in moyamoya disease. *J Neurosurg Anesthesiol*. 1999;11:25–30.

A.6. What is the role of preoperative embolization therapy?

Highly vascular tumors, especially those that are anatomically difficult to access, present a high risk for substantial intraoperative bleeding. In addition to the systemic risks associated with gross blood loss, surgical exposure can be severely compromised and neuronal and neurovascular inflammation and irritation can be exacerbated by excessive tracking of blood into brain tissue.

To reduce this risk, patients often undergo embolization of the vessels feeding the tumor in the days immediately before surgery. An arterial catheter is inserted, usually in the femoral artery, and guided under fluoroscopy until it rests in any of the vessels that have evolved to supply only the tumor and not normal brain. At this point, a viscous embolic agent is slowly delivered to occlude the vessel, reducing its vascular supply, and thus the degree of bleeding during the operative resection. Because of collateralization and reestablishment of blood supply, embolization is effective for only a short period and is usually performed within 48 hours before the intracranial resection. Tumor embolization comes with its own risks and challenges: Vascular anatomy might not always permit embolization, and the embolization itself can precipitate swelling around the tumor and hyperemic changes in blood flow dynamics. These changes are particularly relevant in this patient with a posterior fossa tumor proximate to the brainstem. Deposition of embolic agent into vessels supplying normal brain amounts to an embolic stroke can have catastrophic consequences. Further, embolizations almost always require general anesthesia, and thus assume all of the associated general and neurospecific risks.

Carli DF, Sluzewski M, Beute GN, et al. Complications of particle embolization of meningiomas: frequency, risk factors, and outcome. *AJNR Am J Neuroradiol*. 2010;31:152–154.

Dowd CF, Halbach VV, Higashida RT. Meningiomas: the role of preoperative angiography and embolization. *Neurosurg Focus*. 2003;15:E10.

Young WL. Anesthesia for endovascular neurosurgery and interventional neuroradiology. *Anesthesiol Clin.* 2007;25:391–3412.

B. Preoperative Evaluation and Preparation

B.1. What are special considerations in preoperative evaluation of the patient scheduled for posterior fossa craniotomy?

In addition to the routine thorough preoperative evaluation, the evaluation of the patient for craniotomy should answer several questions that critically influence anesthesia management:

- What is the ICP? If ICP is still in the normal range, how much intracranial compliance reserve is likely to exist?
- How is autoregulation likely to be affected by the pathology and chronic changes in blood pressure? What range of arterial pressures will be required to preserve adequate CPP and CBF?
- Does the patient have any of the electrolyte and endocrine abnormalities associated with intracranial pathology or treatment, such as neurogenic diabetes insipidus, or hypernatremia resulting from hypertonic saline therapy?
- Is the lesion highly vascular, difficult to access, or situated proximate to one of the large draining veins—all of which increase the probability of significant bleeding?
- What is the likely positioning, and does it incur a risk of venous air embolism, obstruction of jugular venous outflow, or neck hyperextension?
- Is the tumor located in a position close to the brainstem such that severe autonomic dynamics are likely?
- Will the baseline neurologic status affect the ability to extubate or to establish an early neurologic assessment after general anesthesia?
- Will the anesthetic technique need to accommodate specific monitoring requirements, such as electroencephalography (EEG), electrocorticography, BAERs, or SEPs?

Fischer SP. Preoperative evaluation of the adult neurosurgical patient. *Int Anesthesiol Clin.* 1996;34:21–32.

Jellish WS, Murdoch J, Leonetti JP. Perioperative management of complex skull base surgery: the anesthesiologist's point of view. *Neurosurg Focus.* 2002;12:E5.

Lieb K, Selim M. Preoperative evaluation of patients with neurological disease. *Semin Neurol.* 2008;28:603–610.

B.2. In a patient who presents with intracranial hypertension, what management might have already been initiated preoperatively and what are the implications for anesthetic management?

A patient with evidence of intracranial hypertension will be aggressively monitored and treated preoperatively; it is likely that the preoperative assessment will occur in an intensive care setting. The anesthesiologist must be familiar with the management of intracranial hypertension. These therapies will likely need to be initiated or continued in the operating room. Further, the anesthesiologist must be mindful of potential sequelae that can arise from various perioperative therapies and interventions such as:

- *Corticosteroids*. They can result in hyperglycemia, which should be aggressively treated to maintain plasma glucose less than 150 to 180 mg/dL.

- *Head elevation*. Care should be taken to avoid rapidly lowering the head during transport.
- *Diuretics (mannitol, furosemide)*. These can result in electrolyte or acid–base abnormalities. Decreased preload can increase the risk of hypotension in the peri-induction period.
- *Isotonic or hypertonic saline therapy*. This can result in hypernatremia or a hyperchloremic, non–anion gap metabolic acidosis.
- *Intubation and institution of hyperventilation*. If prolonged, CBF response can be diminished or absent, with risk for increase in CBF and ICP if hyperventilation is rapidly ceased. It can lead to underlying compensatory metabolic acidosis. Care should be taken to avoid hypoventilation during transport.
- *Ventriculostomy*. This is usually clamped during transport to or from the ICU, as the level of the drain relative to the head is critical, and accidental changes in position can result in excessive draining of CSF. It should be attended to on arrival to the operating room, because even relatively short periods of clamping can result in elevations of ICP.
- *Manipulation of systemic pressures to optimize CPP*. Care should be taken to ensure drug infusions are maintained during transport to avoid rebound hypertension or hypotension.
- *Drug-induced cerebral vasoconstriction and coma*. Thiopental is usually used. This signifies a critical neurologic status. The therapy is often continued as the primary anesthetic.
- *Deliberate hypothermia*. This signifies a critical neurologic status. Requires discussion of intraoperative temperature management goals with the neurosurgeon and neurointensivist, because the neuroprotective benefits may be countered by hypothermia-induced coagulopathy.

Li LM, Timofeev I, Czosnyka M. Review article: the surgical approach to the management of increased intracranial pressure after traumatic brain injury. *Anesth Analg.* 2010;111:736–748.

Stevens RD, Bhardwaj A. Evolving paradigms in the management of severe traumatic brain injury. *Crit Care Med.* 2005;33:2415–2417.

Vincent JL, Berre J. Primer on medical management of severe brain injury. *Crit Care Med.* 2005;33:1392–1399.

B.3. How will intraoperative electromyography (EMG), sensory evoked potential (SEP), or brainstem auditory evoked response (BAER) monitoring affect the anesthetic management plan?

The most common EMG monitoring during posterior fossa surgery is for cranial nerve VII, although monitoring of V, IX, X, and XI is frequently encountered. Usually, the surgeon will deliver a very low current to a structure they believe could be the cranial nerve of interest, and muscular activity is monitored in the distribution of the nerve; mechanical manipulation of a nerve will often also cause muscular activity. Therefore, during EMG monitoring, neuromuscular blockers should not be used beyond the anesthetic induction. Some anesthesiologists advocate the use of succinylcholine for intubation; nevertheless, a low intubating dose of a medium-duration nondepolarizing agent such as vecuronium or cisatracurium allows adequate return of muscular function by the time monitoring is relevant and avoids the issues associated with succinylcholine.

The most common evoked potential monitoring encountered during resection of posterior fossa tumors is the BAER, which monitors cranial nerve VIII. Somatosensory evoked potentials (SSEPs) can also be used to monitor cortical integrity. Although BAERs are reasonably robust, many common anesthetic drugs cause decreases in

amplitude and increases in latency of the evoked responses, thereby mimicking neuronal ischemia or trauma. Volatile agents should be kept at less than 0.5 MAC, and nitrous oxide should not be used. The anesthetic plan will often rely heavily on opioids; propofol and dexmedetomidine infusions are also often incorporated, the latter of which may also offer improvements in overall hemodynamic stability. Perhaps more important than the specific anesthetic regimen is that a maintenance equilibrium is established for the baseline neurophysiology measurements and is then kept constant throughout the procedure. Pseudo-equilibrated steady-state continuous infusions are key to this strategy.

Bala E, Sessler DI, Nair DR, et al. Motor and somatosensory evoked potentials are well maintained in patients given dexmedetomidine during spine surgery. *Anesthesiology*. 2008;109:417–425.

Deiner S. Highlights of anesthetic considerations for intraoperative neuromonitoring. *Semin Cardiothorac Vasc Anesth*. 2010;14:51–53.

Harper CM. Intraoperative cranial nerve monitoring. *Muscle Nerve*. 2004;29:339–351.

Lotto ML, Banoub M, Schubert A. Effects of anesthetic agents and physiologic changes on intraoperative motor evoked potentials. *J Neurosurg Anesthesiol*. 2004;16:32–42.

B.4. What are the options for patient positioning during posterior fossa surgery?

- *Sitting position*. Although used far less often now than two decades ago, it is critically important for the anesthesiologist to understand the sitting position: partly because it could still be encountered and partly because it provides the archetype for the risks and management of venous air embolism. The patient is in a reclined sitting posture such that the feet are at or near the level of the heart. The head is held in a flexed position with a skull fixation device, and the arms are crossed over the chest.
- *Prone position*. This is especially suitable for lesions in the midline, but can be adapted for more lateral approaches by having the head slightly rotated. Depending on body habitus, supporting rolls are placed horizontally across the chest and hips or in parallel along the longitudinal axis of the body. The head is held with a skull fixation device with the neck in a neutral to flexed position.
- *Lateral decubitus position*. This position is suited to cerebellopontine angle tumors and cerebellar hemispheric lesions.
- *Park bench (semiprone) position*. The patient is turned toward a more prone position, moving the upper shoulder out of the surgeon's view and permitting better access to midline lesions.
- *Supine position*. This can sometimes be used with the patient's head rotated. To reduce the amount of rotation of the neck, which can obstruct venous outflow, a supporting roll can be placed under the ipsilateral shoulder and the whole bed rotated away from the surgeon.

B.5. What are the principal disadvantages associated with the common posterior fossa craniotomy positions?

In the sitting position, the head is elevated well above the right atrium and usually greater than the height of the central venous fluid column. This will reduce venous bleeding; it will also enable large volumes of air to be entrained into the central venous circulation, especially through the large dural sinuses, which are tented open. When propagated to the right heart and pulmonary circulation, venous air embolism can range in severity from subclinical to severe, precipitating acute hemodynamic

collapse and death. In a patient with a patent foramen ovale—which can exist undetected—air can traverse to the arterial circulation, causing embolic strokes. Although venous air embolism can occur with other positions, the risk and severity are substantially higher in the sitting position. The risk is such that a right heart catheter, with the tip situated precisely at the entrance to the right atrium, is regarded by many neuroanesthesiologists as obligatory. Nonetheless, the placement of these catheters, which might not otherwise be required, incurs associated risks of pneumothorax, infection, bleeding, and arrhythmias and is of limited utility unless the placement is accurate (simple routine placement of a central line rarely offers benefit). Indeed, the treatment of venous air embolism is complicated by the sitting position, because it is difficult to rapidly move the patient's head below the level of the heart. The sitting position is also associated with increased hypotension. As neurosurgeons have gained experience in accessing the posterior fossa from other positions, the risks associated with the sitting position have caused its popularity to dramatically decrease.

In the prone position, the head is usually slightly elevated above the heart; therefore, the risk of venous air embolism is present, although the risk of massive entrainment is much less than in the sitting position. Prone positioning can cause a significant decrease in pulmonary compliance and will increase ventilation–perfusion mismatch, leading to atelectasis, venous admixture, and shunting. Virtually no access is available to the airway, chest, or limbs, and in the event of an airway, pulmonary, or cardiovascular emergency, the prone position places the anesthesiologist in a substantially compromised position.

The supine position alleviates many of these issues. Nevertheless, to access even the lateral posterior fossa from the supine position usually requires substantial rotation of the neck. This can cause obstruction of jugular venous outflow, leading to cerebral venous engorgement, with potentially undesirable effects on ICP, CPP, surgical exposure, and bleeding. The neck rotation can also cause brachial plexus injury as well as significant pressure on laryngeal structures with potential vocal cord injury. Placing supports to elevate the ipsilateral shoulder can reduce rotation at the neck.

Black S, Ockert DB, Oliver WC Jr, et al. Outcome following posterior fossa craniectomy in patients in the sitting or horizontal positions. *Anesthesiology.* 1988;69:49–56.

Fathi AR, Eshtehardi P, Meier B. Patent foramen ovale and neurosurgery in sitting position: a systematic review. *Br J Anaesth.* 2009;102:588–596.

Leslie K, Hui R, Kaye AH. Venous air embolism and the sitting position: a case series. *J Clin Neurosci.* 2006;13:419–422.

Porter JM, Pidgeon C, Cunningham AJ. The sitting position in neurosurgery: a critical appraisal. *Br J Anaesth.* 1999;82:117–128.

Rath GP, Bithal PK, Chaturvedi A, et al. Complications related to positioning in posterior fossa craniectomy. *J Clin Neurosci.* 2007;14:520–525.

B.6. How should the patient position ultimately be determined?

Surgical exposure must determine the first preference for patient position. Nonetheless, the interruption of a posterior fossa craniotomy for anesthesia crisis management poses extreme risk, and thus the anesthesiologist is obligated to discuss concerns with the neurosurgeon and advocate alternative positioning if appropriate. One approach is to trial the preferred position before commencing any surgical management. For example, a patient with compromised pulmonary compliance or reserve can be positioned prone and monitored during other preparations, with alternative positioning sought if the trial fails. The risk of venous air embolism is such that we are very reluctant to use the sitting position except where the surgical exposure considerations are overwhelming.

B.7. How does the sitting position affect your preoperative assessment and planning?

The first step is to establish whether the patient has any contraindications to the sitting position that might have been overlooked. The presence of intracardiac defects, pulmonary arteriovenous malformations, or carotid artery stenosis should be sought. The presence of a patent foramen ovale can lead to a catastrophic paradoxical air embolus if air is entrained; therefore, some neuroanesthesiologists advocate routine preoperative echocardiography if the sitting position is to be used, although in practice this is not commonly performed. The presence of any of these comorbidities—especially the presence of a right-to-left intracardiac shunt—argues against the sitting position, and a thorough risk–benefit assessment must be discussed with the neurosurgeon. Severe hypovolemia, cachexia, and extremes of age can diminish the ability of autonomic reflexes to maintain adequate cerebral and upper lung perfusion in the upright position, making intraoperative cardiopulmonary management extremely difficult. It must be remembered that the critical pressure is the CPP, not the MAP, and that blood pressure must therefore be evaluated at the level of the head. MAPs will need to be higher than would be required in the horizontal positions.

Anesthetic planning must recognize the physiologic implications of the sitting position. Venous pooling will result in lower left atrial filling pressures, leading to reduced stroke volume and cardiac output. Although there will be an increase in both systemic and pulmonary vascular resistance, the net effect is a tendency to arterial hypotension, with decreased CPP. The temptation to counter reduced preload with intraoperative fluid administration could run counter to attempts to diurese and result in an exaggerated increase in cardiac filling when the patient is repositioned supine at the conclusion of surgery. Conversely, because the hypotension is not the result of afterload reduction, use of vasopressors, while increasing arterial pressures, can reduce end-organ blood flow. Because of the beneficial effects of gravity, pulmonary compliance and functional residual capacity are greater in the sitting position than in horizontal positions; the simultaneous cardiovascular effects can lead to increased ventilation-perfusion mismatch, countering any significant benefit.

If the sitting position is to be used, there must be a preoperative plan for the detection and management of venous air embolism, should it occur. The patient's neck must be evaluated for any difficulties in the placement of a right atrial catheter. In some patients—such as those who have previously had chemotherapy or dialysis through central catheters, have received neck irradiation, or are morbidly obese—emergent placement of a right atrial catheter can be extremely difficult or impossible. This necessitates the consideration of alternative positions or preoperative radiologically guided placement.

Gale T, Leslie K. Anaesthesia for neurosurgery in the sitting position. *J Clin Neurosci*. 2004;11:693–696.

Kwapisz MM, Deinsberger W, Muller M, et al. Transesophageal echocardiography as a guide for patient positioning before neurosurgical procedures in semi-sitting position. *J Neurosurg Anesthesiol*. 2004;16:277–281.

Stendel R, Gramm HJ, Schroder K, et al. Transcranial Doppler ultrasonography as a screening technique for detection of a patent foramen ovale before surgery in the sitting position. *Anesthesiology*. 2000;93:971–975.

B.8. Should this patient receive premedication?

A professional and unrushed visit by the anesthesiologist is the optimal approach to preoperative anxiolysis. With rare exceptions, pharmacologic approaches to anxiolytic, sedative, and analgesic premedication should be avoided or restricted to

short-acting agents in patients with intracranial pathology. It is absolutely critical to be able to assess whether a failure to emerge from anesthesia is the result of pharmacologic sensitivity or neurologic injury, and residual effects from benzodiazepines and other psychoactive drugs can confound the ability to accurately assess changes in the neurologic examination. Opioids will precipitate some degree of hypoventilation, leading to hypercapnia and a consequent increased CBF and CBV. In a patient with minimal intracranial compliance reserve, such as this patient, even a small increase in CBV secondary to hypoventilation might precipitate a dangerous increase in ICP. Preinduction opioid dosing should be performed only with complete monitoring and under the direct supervision of an anesthesiologist who is able to rapidly intervene and take over ventilation. Oral dosing of gabapentin and clonidine will attenuate the hemodynamic instability resulting from laryngoscopy and head pinning when given before anesthetic induction. The effects of clonidine can likely be mimicked by starting an infusion of dexmedetomidine—also an α_2-adrenergic agonist—as soon as the patient arrives in the operating room.

Costello TG, Cormack JR. Clonidine premedication decreases hemodynamic responses to pin head-holder application during craniotomy. *Anesth Analg*. 1998;86:1001–1004.

Misra S, Koshy T, Suneel PR. Oral clonidine attenuates the fall in mean arterial pressure due to scalp infiltration with epinephrine-lidocaine solution in patients undergoing craniotomy: a prospective, randomized, double-blind, and placebo controlled trial. *J Neurosurg Anesthesiol*. 2009;21:297–301.

Misra S, Koshy T, Unnikrishnan KP, et al. Gabapentin premedication decreases the hemodynamic response to skull pin insertion in patients undergoing craniotomy. *J Neurosurg Anesthesiol*. 2010;doi:10.1097/ANA.0b013e3181da3c3b.

C. Intraoperative Management

C.1. What are the anesthetic goals for craniotomy?

Clearly the anesthetic goals for craniotomy include the basic principles of physiologic stability that are common to all anesthetic management. Craniotomy incurs several specific goals that follow from the effects—both helpful and unhelpful—of anesthetic drugs on the brain. Stated succinctly, the anesthetic goals specific to craniotomy are to protect the brain from injury resulting from mechanical or physiologic insult during the perioperative period. *Direct* protection (often referred to simply as *neuroprotection*) can be conceptualized as actions that facilitate the ability of neural tissue to withstand ischemic episodes without neurosis or activation of the apoptotic cascade leading to infarction. Less discrete is the concept of *indirect* protection, which aims to minimize the anteceding ischemic episodes. The principal elements are as follows:

- Management of CBF and CPP
- Management of ICP while the skull is intact
- The provision of a "relaxed" brain. This optimizes surgical exposure, which is critically important in many cases because the field of view available to the surgeon in many craniotomy approaches can be extremely narrow. Further, relaxation reduces the pressure—resulting in ischemia exerted by the retraction devices on underlying brain tissue
- Implementation and timing of pharmacologic measures specifically intended to effect direct neuroprotection, traditionally involving anesthetic-induced induction of a burst-suppression pattern on the EEG (although experimental data suggest that anesthetics can be protective without burst suppression)
- Strict management of physiologic parameters that may contribute to brain injury, such as serum glucose, osmolarity, and acid–base balance

- Minimize the effect of anesthetic pharmacology, cerebral perfusion, and temperature on neurophysiologic monitoring, such as EEG, BAERs, or SSEPs
- Facilitate early neurologic assessment

Bhagat H, Dash HH, Bithal PK, et al. Planning for early emergence in neurosurgical patients: a randomized prospective trial of low-dose anesthetics. *Anesth Analg* 2008;107:1348–1355.

Citerio G, Franzosi MG, Latini R, et al. Anaesthesiological strategies in elective craniotomy: randomized, equivalence, open trial—the NeuroMorfeo trial. *Trials*. 2009;10:19.

Leslie K, Troedel S. Does anaesthesia care affect the outcome following craniotomy? *J Clin Neurosci*. 2002;9:231–236.

Mantz J, Degos V, Laigle C. Recent advances in pharmacologic neuroprotection. *Eur J Anaesthesiol*. 2010;27:6–10.

Pasternak JJ, Lanier WL. Neuroanesthesiology update. *J Neurosurg Anesthesiol*. 2010;22:86–109.

C.2. What monitors should be used during craniotomy?

As with all patients undergoing general anesthesia, monitoring must include electrocardiography, blood pressure, pulse oximetry, temperature, and capnography. Placement of an arterial line is routine for tumor craniotomies and should be regarded as mandatory for everything except the most superficial and nonvascular supratentorial tumors. The case for arterial line placement is not restricted to hemodynamic arguments, because access to arterial blood for monitoring of carbon dioxide, glucose, acid–base physiology, and electrolytes usually affects management. Arterial lines can often be placed following induction, but are appropriate before induction in patients with significantly deranged autoregulation or minimal intracranial compliance reserve. In such patients, CBF and CPP are pressure dependent during this highly dynamic period. Clearly, other comorbidities also necessitate placement of a preinduction arterial line. The transducer should be set to zero at the level of the circle of Willis, which in sitting or semisitting positions is significantly higher than the level of the heart. The decision on whether to place a central venous line for CVP or right heart monitoring is generally determined by the patient's overall physiologic state; it usually offers very little, if any, benefit in the majority of patients. One notable exception is during posterior fossa procedures in the sitting position. Central access is required for the administration of some drugs, such as hypertonic saline.

In any case with risk for a venous air embolism, precordial Doppler monitoring or some other detection method such as transesophageal echocardiography or end-tidal N_2 monitoring should be used. That said, our experience is that suboptimal placement conditions and the high degree of interference render the precordial Doppler inadequately sensitive or specific, and it must be interpreted in the context of $ETco_2$ and hemodynamic parameters. The use of neurophysiology monitoring such as EEG, EMG, BAERs, or SSEPs is determined by the location of the tumor; although these methods are often performed by neurophysiologists, the anesthesiologist must understand the principles behind them and be aware of the effects of anesthetics, other drugs, and physiologic variables on their integrity.

C.3. What specific risks are associated with induction of anesthesia?

The patient with intracranial pathology will have a diminished ability to tolerate or compensate for the hemodynamic changes that can occur during induction. Hypotension can result in inadequate CPP and precipitate hypoperfusion cerebral ischemia in brain tissue that already has marginal perfusion, whereas hypertension and sympathetic activation can precipitate hyperemia, increased CBF and CBV, and

consequently increased ICP. Implications of rapid changes in $Paco_2$ are often underappreciated: high-dose opioids are frequently used to blunt the sympathetic response to laryngoscopy and to reduce the required MAC fraction of volatile agents. When given before induction, opioids can precipitate hypoventilation and an acute increase in $Paco_2$, leading to increased CBF and CBV. Significant doses of opioids should never be administered until the patient is under direct care of the anesthesiologist, because this increase in CBV may be sufficient to lead to decompensation in a patient with minimal ICP reserve. Episodes of coughing, especially relevant if the airway has to be secured by an awake technique, precipitate short but dramatic increases in ICP and cannot be tolerated. Hypoxia will be very poorly tolerated by brain tissue with marginal reserve.

Lanier WL, Albrecht RF 2nd, Laizzo PA. Divergence of intracranial and central venous pressures in lightly anesthetized, tracheally intubated dogs that move in response to a noxious stimulus. *Anesthesiology.* 1996;84:605–613.

C.4. How would you induce anesthesia?

To a large extent, the specific drug combinations used during induction are probably less important than the ultimate goal of maintaining tight hemodynamic stability during the peri-induction period. Dexmedetomidine can reduce hemodynamic instability during craniotomy and might afford some degree of neuroprotection. Because of its pharmacokinetics, one favored approach is to begin a dexmedetomidine infusion as soon as possible after the patient enters the operating room. The use of midazolam or another benzodiazepine as an anxiolytic and amnestic is frequently questionable, because its prolonged elimination has the potential to delay emergence and cloud the early neurologic examination in a patient with reduced cognitive reserve, especially after the additional insult of a retracted and handled brain. It should certainly not be used in elderly patients or those who already exhibit compromised neurologic function.

With adequate ventilation, the use of high-dose opioids during induction (e.g., fentanyl slowly titrated to a total dose of 5 to 10 μg per kg) offers many advantages: The sympathetic response to laryngoscopy and head pinning is blunted, and the requirement for other anesthetics is reduced. If the anesthetic plan involves the use of a volatile anesthetic, this latter point is of particular significance, because concentrations of volatile anesthetics should be kept low to avoid the undesirable effect of increased CBV, leading to elevated ICP. With high-dose opioid techniques, the airway can usually be taken over by the addition of a small dose of propofol, which serves as an excellent amnestic. A volatile anesthetic agent can be added to create a mixed intravenous-inhalational induction, but because of the effects on CBV (discussed later), caution should be used to keep values less than 1 MAC. Etomidate should be considered in patients with significant cardiac comorbidities or who are otherwise critically ill. A nondepolarizing muscle relaxant should be used for intubation; succinylcholine is not absolutely contraindicated, but because it can cause a transient increase in ICP, an effect that can be minimized by coadministration of lidocaine, its use should be reserved for situations in which it is strongly indicated. Although hypoventilation is obviously undesirable, care should also be taken to avoid excessive hyperventilation, because it can reduce CBF sufficient to cause hypoperfusion and ischemia.

This induction strategy, as with most others, incurs the risk of decreasing systemic vascular resistance and precipitating hypotension. In patients who are highly dependent on sympathetic vascular tone, the effective sympathectomy created by high-dose opioids can lead to hypotension, even if the need for drugs with direct vasodilatory properties—such as propofol or the volatile agents—is reduced.

The use of phenylephrine 40 to 120 μg during induction can be helpful. Alternatively, if high-dose opioids are not desired, lidocaine 1.5 mg per kg can be given 1 to 2 minutes before laryngoscopy and head pinning.

Bekker AY, Mistry A, Ritter AA, et al. Computer simulation of intracranial pressure changes during induction of anesthesia: comparison of thiopental, propofol, and etomidate. *J Neurosurg Anesthesiol.* 1999;11:69–80.

Bekker A, Sturaitis M, Bloom M, et al. The effect of dexmedetomidine on perioperative hemodynamics in patients undergoing craniotomy. *Anesth Analg.* 2008;107:1340–1347.

Bozeman WP, Idris AH. Intracranial pressure changes during rapid sequence intubation: a swine model. *J Trauma.* 2005;58:278–283.

C.5. What are the effects of anesthetics on cerebral metabolic rate of oxygen ($CMRO_2$), CBF, and ICP? With this in mind, how would you maintain anesthesia?

Volatile Anesthetics

All volatile anesthetics reduce $CMRO_2$, with isoflurane having the most substantial effect at normal clinical doses. At concentrations up to 1 MAC, some degree of autoregulation is maintained such that there is a relationship between $CMRO_2$ and CBF. Nevertheless, volatile agents also have a direct vasodilatory effect, and at any given $CMRO_2$ the CBF will increase with increasing concentration of anesthetic agent. This effect is exaggerated at concentrations exceeding 1 MAC. The net result is that, despite a decrease in $CMRO_2$, there is an overall increase in CBF, greater in deeper structures than in the cerebral cortex. In most patients, this increased CBF would be potentially beneficial to the extent that it improves the supply–demand balance (often termed *luxury perfusion*). Nevertheless, in patients with intracranial pathology, this increase in CBF causes an increase in CBV and potentially elevation in ICP while the cranial bone is intact or can impede surgical exposure once the bone plate is removed. Finally, $PaCO_2$ reactivity is preserved in healthy brain at concentrations less than 1 MAC, but pathologic brain can have diminished or absent carbon dioxide responsiveness.

Nitrous Oxide

Studies have shown substantial variation in the effects of nitrous oxide (N_2O), which probably relates to the heterogeneity of the anesthetic combinations in which it has been studied. The balance of evidence suggests that N_2O increases $CMRO_2$, CBF, and ICP. ICP increases can be marked, especially if used in combination with a volatile agent; the effect can be attenuated by the addition of an intravenous anesthetic. At best, N_2O offers no neuroprotection, and at worst, its effects might be neurotoxic and counterproductive to surgical exposure. The use of N_2O has also been shown to worsen outcomes of other perioperative complications, including wound infection and deep venous thrombosis. With availability of alternative short-acting intravenous, volatile, and opioid anesthetics, N_2O is relatively contraindicated in craniotomy for intracranial pathology.

Intravenous Anesthetics

The intravenous anesthetics that act through GABAergic mechanisms (e.g., barbiturates, propofol, etomidate) cause a dose-dependent reduction in $CMRO_2$, CBF, CBV, and ICP. In contrast to volatile anesthetics, CBF–$CMRO_2$ coupling is preserved in the basal state, with no added vasodilatory effect. Thus, the direct drug effect of a drug such as propofol is to cause a reduction in $CMRO_2$, and the decreases in CBF, CBV, and ICP follow from intact normal physiologic responses. Carbon dioxide reactivity is preserved. $CMRO_2$ can be reduced to as low as 40% of resting values in the presence of

an isoelectric EEG. The preservation of CBF–$CMRO_2$ coupling affords many benefits, but also carries an underappreciated risk: If hyperventilation is instituted, it will have an additive effect on the decreases in CBF caused by an intravenous anesthetic. The result is an appreciable risk of inadequate CBF and hypoperfusion ischemia. It must be remembered that the mantra of "craniotomy → hyperventilation" owes its legacy to a time when most neuroanesthetics involved the use of MAC equivalents of vasodilating volatile agents. Etomidate can impair collateral perfusion of ischemic brain in animal experiments through inhibition of nitric oxide synthase and is thus relatively contraindicated in cerebral ischemia.

The N-methyl-D-aspartic acid (NMDA)-antagonist ketamine can increase $CMRO_2$, CBF, and ICP, although in small doses concerns about these effects are probably overstated. Indeed, while ketamine may change the oxygen supply–demand relationship in an adverse way, recent studies suggest that ketamine possesses direct neuroprotective effects, especially when combined with GABAergic agents. There is no definitive evaluation of its clinical use; nevertheless, judicious use of ketamine can probably be justified where there are appropriate indications.

Opioids

The effects of opioid drugs on $CMRO_2$, CBF, and ICP are generally far less significant than those of other intravenous or gaseous anesthetics. Most evidence suggests that opioids have no effect or only slightly reduce $CMRO_2$, CBF, and ICP. In the awake patient, opioids cause hypoventilation, elevated $PaCO_2$, and a consequent increase in CBF and potentially in ICP. As discussed earlier, vigilance must be maintained during preinduction sedation and in the immediate postextubation period.

Many neuroanesthesiologists favor a maintenance strategy of total intravenous anesthesia (TIVA) in an oxygen and air mixture, which is difficult to fault provided that hyperventilation is not excessive. A TIVA approach maximizes the ability to reduce $CMRO_2$ without impairing surgical exposure through increased CBF or causing cerebral steal, but it incurs the disadvantage of complex pharmacokinetics. Other neuroanesthesiologists (including the authors) favor a mixed volatile-intravenous regimen as a primary strategy in most patients. We typically use 0.3 to 0.5 MAC equivalent of a volatile agent, with propofol titrated to the EEG as an endpoint. Dexmedetomidine and (usually high-dose) opioids are added to blunt hemodynamic responses and confer hemodynamic stability. This strategy causes a reduction in $CMRO_2$, but with minimal impairment of surgical exposure. Unless precluded by monitoring, a nondepolarizing muscle relaxant is added to ensure that the patient does not move while the head is fixed. We revert to TIVA if there is inadequate brain relaxation or if monitoring dictates.

Fraga M, Rama-Maceiras P, Rodino S, et al. The effects of isoflurane and desflurane on intracranial pressure, cerebral perfusion pressure, and cerebral arteriovenous oxygen content difference in normocapnic patients with supratentorial brain tumors. *Anesthesiology*. 2003;98:1085–1090.

Guy J, Hindman BJ, Baker KZ, et al. Comparison of remifentanil and fentanyl in patients undergoing craniotomy for supratentorial space-occupying lesions. *Anesthesiology*. 1997;86:514–524.

Hudetz JA, Pagel PS. Neuroprotection by ketamine: a review of the experimental and clinical evidence. *J Cardiothorac Vasc Anesth*. 2010;24:131–142.

Lehmberg J, Waldner M, Baethmann A, et al. Inflammatory response to nitrous oxide in the central nervous system. *Brain Res*. 2008;1246:88–95.

Maurtua MA, Deogaonkar A, Bakri MH, et al. Dosing of remifentanil to prevent movement during craniotomy in the absence of neuromuscular blockade. *J Neurosurg Anesthesiol*. 2008;20:221–225.

Myles PS, Leslie K, Chan MT, et al. Avoidance of nitrous oxide for patients undergoing major surgery: a randomized controlled trial. *Anesthesiology*. 2007;107:221–231.

Petersen KD, Landsfeldt U, Cold GE, et al. Intracranial pressure and cerebral hemodynamic in patients with cerebral tumors: a randomized prospective study of patients subjected to craniotomy in propofol-fentanyl, isoflurane-fentanyl, or sevoflurane-fentanyl anesthesia. *Anesthesiology*. 2003;98:329–336.

Rasmussen M, Juul N, Christensen SM, et al. Cerebral blood flow, blood volume, and mean transit time responses to propofol and indomethacin in peritumor and contralateral brain regions: perioperative perfusion-weighted magnetic resonance imaging in patients with brain tumors. *Anesthesiology*. 2010;112:50–56.

C.6. How would you manage ventilation and maintain arterial carbon dioxide?

A reduction of $Paco_2$ decreases CBF and CBV within minutes. Therefore, hyperventilation is a rapidly effective measure that can be instituted to decrease ICP and undoubtedly can improve surgical exposure. Nevertheless, hyperventilation has substantial limitations. At $Paco_2$ values less than 25 mm Hg, cerebral ischemia can result from a critical reduction in CBF combined with impaired oxygen unloading caused by a large left shift of the oxyhemoglobin dissociation curve resulting from respiratory alkalosis. Prolonged hyperventilation results in metabolic acidosis through normal compensatory mechanisms and can result in rebound acidosis if hyperventilation is rapidly terminated. Further, hyperventilation-induced alkalosis decreases in ionized Ca^{2+}, leading to hemodynamic difficulties and prolonged emergence from effects on synaptic function.

It is important to remember that the difference between $Paco_2$ and $ETco_2$ can vary greatly. Therefore, arterial blood gas analysis should be performed as soon as possible after induction to establish the arterial–end-tidal gradient in carbon dioxide partial pressure. A $Paco_2$ of approximately 35 mm Hg is reasonable unless ICP is elevated. If, once the bone plate is removed, the surgeons determine that exposure is suboptimal, hyperventilation to a $Paco_2$ of 30 mm Hg is usually helpful. Further hyperventilation is reserved for situations in which establishing adequate exposure is extremely difficult. To avoid postoperative acid–base instability, hyperventilation can be gradually reduced throughout the closure, permitting reestablishment of bicarbonate and Ca^{2+} equilibrium.

Brian JE Jr. Carbon dioxide and the cerebral circulation. *Anesthesiology*. 1998;88:1365–1386.

Curley G, Kavanagh BP, Laffey JG. Hypocapnia and the injured brain: more harm than benefit. *Crit Care Med*. 2010;38:1348–1359.

Gelb AW, Craen RA, Rao GS, et al. Does hyperventilation improve operating condition during supratentorial craniotomy? A multicenter randomized crossover trial. *Anesth Analg*. 2008;106:585–594.

Meyer MJ, Megyesi J, Meythaler J, et al. Acute management of acquired brain injury (part I): an evidence-based review of non-pharmacological interventions. *Brain Inj*. 2010;24:694–705.

C.7. How would you approach diuretic therapy?

The purpose of diuretic therapy in intracranial procedures is to dehydrate the brain, thereby leading to a reduction in the volume of the fluid compartment. This facilitates surgical exposure and reduces the requirement for brain retraction. Through the same principal, mannitol is used as therapy for elevated ICP states when the cranium is closed.

Mannitol is an osmotic diuretic that is usually prepared in a 20% solution (20 g per 100 mL). It should initially be given in a dose of 0.5 to 1 g per kg; the total dose

can be increased to 1.5 g per kg if initial efforts are ineffective. Higher doses have been reported to lead to cardiac arrest from disruption of cardiac cellular function. Because mannitol initially draws water into the vascular space before it is excreted, rapid dosing can cause a transient increase in ICP, so it should be infused over 20 to 30 minutes. If there is very little intracranial compliance reserve, aggressive dosing should be synchronized with the removal of the bone plate.

If mannitol does not provide adequate surgical conditions, the loop diuretic furosemide can be used. In a naïve adult patient, a dose as low as 5 mg might be adequate. Furosemide does not have the problem of an initial increase in vascular volume and so is preferred in patients with marginal cardiac function who can develop congestive heart failure with a large mannitol load. The combination of mannitol and furosemide can cause electrolyte abnormalities and severe systemic dehydration, necessitating fluid resuscitation. Because mannitol therapy alone is often adequate, we do not administer furosemide routinely, instead reserving its use for situations when surgical exposure is suboptimal.

In cases of extreme cerebral edema, hypertonic saline in concentrations of up to 20% can be used—although the most common concentrations used are 2% or 3%. This can be effective in refractory intracranial hypertension and might even be superior to mannitol for routine diuresis. Its use requires caution because of the risk of severe hypernatremia, and central access is required. Thus, it is relatively unusual for hypertonic saline to be initiated intraoperatively. Patients who are already receiving hypertonic saline should usually have the infusion maintained during the operative period.

Rozet I, Tontisirin N, Muangman S, et al. Effect of equiosmolar solutions of mannitol versus hypertonic saline on intraoperative brain relaxation and electrolyte balance. *Anesthesiology*. 2007;107:697–704.

Thenuwara K, Todd MM, Brian JE Jr. Effect of mannitol and furosemide on plasma osmolality and brain water. *Anesthesiology*. 2002;96:416–421.

Wu CT, Chen LC, Kuo CP, et al. A comparison of 3% hypertonic saline and mannitol for brain relaxation during elective supratentorial brain tumor surgery. *Anesth Analg*. 2010;110:903–907.

C.8. How would you manage serum glucose?

For reasons that are incompletely understood, hyperglycemia worsens both neurologic and nonneurologic critical care outcomes. This is almost universally relevant in patients with intracranial pathology, because even nondiabetic patients undergoing craniotomy are at risk for hyperglycemia secondary to corticosteroid therapy. No study has clearly identified the level of serum glucose that requires intraoperative treatment in craniotomy patients. Nevertheless, extrapolation from the ICU and brain trauma literature suggests that tight glucose control to a serum level of approximately 150 mg per dL is likely to confer benefit and unlikely to cause harm. Although some advocate for even tighter control (with target levels approximately 120 mg per dL), this approach can increase the risk of hypoglycemic episodes, which carry significant morbidity. Glycemic control is too often overlooked in the operating room, where it likely presents a significant opportunity to influence outcomes.

Fahy BG, Sheehy AM, Coursin DB. Glucose control in the intensive care unit. *Crit Care Med*. 2009;37:1769–1676.

Lipshutz AK, Gropper MA. Perioperative glycemic control: an evidence-based review. *Anesthesiology*. 2009;110:408–421.

Lukins MB, Manninen PH. Hyperglycemia in patients administered dexamethasone for craniotomy. *Anesth Analg*. 2005;100:1129–1133.

Rice MJ, Pitkin AD, Coursin DB. Review article: glucose measurement in the operating room: more complicated than it seems. *Anesth Analg.* 2010;110:1056–1065.

Rovlias A, Kotsou S. The influence of hyperglycemia on neurological outcome in patients with severe head injury. *Neurosurgery.* 2000;46:335–342.

C.9. How would you approach fluid management?

If the blood–brain barrier (BBB) is intact, the principal determinant of brain tissue water is the osmotic gradient across the BBB. It is this importance of osmotic gradient that guides the use of hypertonic solutions such as mannitol or hypertonic saline to reduce interstitial water and reduce ICP or to optimize surgical exposure. By the same principle, hypotonic solutions such as lactated Ringer's solution are rarely used because they favor the transport of water into the brain interstitium, thereby promoting the development of edema.

In regions where the BBB is not intact because of pathology and surgical tissue injury, osmotic particles can cross from the capillaries into the interstitial tissue. Therefore, the benefits of hypertonic solutions are lost in these areas. It follows that the benefit obtained from the use of hypertonic solutions is because of an *overall* effect on the brain, not from a *specific* effect in localized regions of brain injury.

These considerations favor the use of isotonic normal (0.9%) saline as maintenance fluid in craniotomies. More controversial is the approach to volume management. Historically, craniotomy patients have been kept deliberately hypovolemic in the belief that this will increase the passage of free water from the brain in situations involving a disrupted BBB. Relatively recent evidence suggests that there is in fact very little reduction in interstitial water, and that it comes at the price of significant systemic hypoperfusion and hypotension. Therefore, the favored approach to fluid management is now maintenance of isovolemia with normal saline. In prolonged cases, the chloride loading can result in mild hyperchloremic non–anion gap metabolic acidosis. Dextrose-containing solutions should never be used except to treat hypoglycemia. Colloids such as 5% albumin can be used when volume expansion is a requirement. Albumin has a plasma half-life of 16 hours, and little is known about how the passage of albumin across a damaged BBB influences interstitial water movement over this time period. Therefore, its routine use is not recommended.

Scheingraber S, Rehm M, Sehmisch C, et al. Rapid saline infusion produces hyperchloremic acidosis in patients undergoing gynecologic surgery. *Anesthesiology.* 1999;90:1265–1270.

C.10. Once the bone plate is removed and the dura retracted, the surgeon reports that the brain is still "tight." What would be your response?

In almost all cases, the most effective initial response is to increase hyperventilation to a $Paco_2$ of approximately 27 to 30 mm Hg. If mannitol 1 g per kg has already been administered, furosemide can be given until a diuresis is established. If a volatile agent is being used, this should be discontinued and the maintenance strategy converted to TIVA. If the patient has a CSF drain, this can be opened and CSF removed in no greater than 10- to 20-mL aliquots, with reassessment in between. Hypertension should be addressed and treated, and the patient should be well anesthetized to attenuate CBF responses to surgical stimulation. Positioning should be reassessed to eliminate any obstruction to jugular venous outflow. Deliberate hypotension can reduce swelling, but incurs the risk of inadequate CPP and hypoperfusion ischemia and is thus instituted sparingly.

C.11. If deliberate hypotension is indicated, how will you achieve it?

Although sodium nitroprusside and volatile anesthetics are historically the most commonly used drugs to achieve sustained decreases in blood pressure, both are very far from ideal. Nitroprusside is highly effective and titratable over extremely short periods, but because it causes cerebral vasodilation, it can actually increase vascular engorgement. Nitroglycerin is also a potent cerebral venous vasodilator, and so it has the same limitation. Similarly, high levels of volatile anesthetic have direct cerebral vasodilatory effects. Further, the uncoupled cerebral vasodilation caused by nitrates and volatile anesthetics can theoretically produce cerebral steal.

In most cases, the required level of blood pressure reduction can be achieved with the use of high-dose remifentanil (or other opioid) and propofol, possibly with the addition of a β- adrenergic blocker. Remifentanil enables a profound but rapidly reversible opioid level without unfavorable effects on CBF or vasodilation. Similarly, propofol can produce hypotension through systemic vasodilation but does not cause cerebral vasodilation and is rapidly reversible. The mixed adrenergic receptor blocker labetalol is often effective as an adjunctive agent. However, the calcium channel blocker nicardipine is probably the most versatile drug for blood pressure control: It is titratable over relatively short periods and is an excellent choice if hypotension is required in situations in which opioids and anesthetic agents are not appropriate—such as during emergence or in the ICU—although it might impair autoregulation. Esmolol infusions can be utilized for a titratable β_1-adrenergic blockade, but are not especially effective if the problem is refractory hypertension. With the advent of these newer drugs, the ganglionic blocker trimethaphan is now rarely used.

Degoute CS. Controlled hypotension: a guide to drug choice. *Drugs*. 2007;67:1053–1076.

Degoute CS, Ray MJ, Manchon M, et al. Remifentanil and controlled hypotension; comparison with nitroprusside or esmolol during tympanoplasty. *Can J Anaesth*. 2001;48:20–27.

Endoh H, Honda T, Ohashi S, et al. The influence of nicardipine-, nitroglycerin-, and prostaglandin E(1)-induced hypotension on cerebral pressure autoregulation in adult patients during propofol-fentanyl anesthesia. *Anesth Analg*. 2002;94:169–173.

Hoffman WE, Edelman G, Ripper R, et al. Sodium nitroprusside compared with isoflurane-induced hypotension: the effects on brain oxygenation and arteriovenous shunting. *Anesth Analg*. 2001;93:166–170.

Narotam PK, Puri V, Roberts JM, et al. Management of hypertensive emergencies in acute brain disease: evaluation of the treatment effects of intravenous nicardipine on cerebral oxygenation. *J Neurosurg*. 2008;109:1065–1074.

Rose JC, Mayer SA. Optimizing blood pressure in neurological emergencies. *Neurocrit Care*. 2004;1:287–299.

C.12. While the surgeon is resecting tumor from near the brainstem, the patient's heart rate suddenly drops to 20 beats per minute. What is your assessment and management?

Surgery near the brainstem nuclei can result in dramatic autonomic disturbances. Profound vagal reflexes can be alarming, sometimes resulting in asystole. These are often followed by a compensatory parasympatholytic-sympathetic reflex. Under such circumstances, the hemodynamics can shift from extreme bradycardia and hypotension to tachycardia and hypertension in a matter of seconds.

The first step is to alert the surgeon to stop operating, which almost always alleviates the problem. Once the hemodynamic status has stabilized, an "autonomic blunting" prophylactic regimen can be given. Glycopyrrolate should be titrated until a 15% to 20%

increase in heart rate is observed; if sympathetic reflexes are also involved, β-adrenergic blockade can be added. This approach is usually effective in attenuating the reflexes. In surgery in which an elevated risk of autonomic instability is present, the institution of parasympatholytic prophylaxis should be strongly considered from the outset.

The sudden development of bradycardia should always alert the anesthesiologist to the possibility of a sudden increase in ICP, leading to the Cushing reflex. In this case, hypertension will be seen and the surgeon should be immediately notified.

Koerbel A, Gharabaghi A, Samii A, et al. Trigeminocardiac reflex during skull base surgery: mechanism and management. *Acta Neurochir (Wien)*. 2005;147:727–733.

Schaller B, Probst R, Strebel S, et al. Trigeminocardiac reflex during surgery in the cerebellopontine angle. *J Neurosurg*. 1999;90:215–220.

C.13. Would you monitor for venous air embolism? What are the monitoring options?

Although the risk of venous air embolism is most marked when the sitting position is used, it can occur whenever the surgical site is farther above the heart than the venous column. This applies in many approaches to the posterior fossa; therefore, some form of monitoring for venous air embolism is recommended, with the caveat that invasiveness should be proportionate to risk.

A precordial Doppler ultrasound transducer, when optimally placed, is highly sensitive and noninvasive. We use it routinely for posterior fossa procedures. Nevertheless, placement over the right heart can be difficult with many positioning configurations and its sensitivity and specificity in many real-world scenarios is suboptimal. The ability to detect turbulent flow should be assessed by rapidly injecting 5 to 10 mL of saline intravenously and listening for the characteristic coarse change in sound quality. The combination of precordial Doppler, $ETCO_2$, and arterial pressure monitoring is extremely effective at detecting clinically significant venous air embolism. Transesophageal echocardiography is extremely sensitive and can detect air bubbles in the left heart, but it requires operator expertise and is often impossible in the horizontal operating positions. End-tidal nitrogen is noninvasive, but can be difficult to interpret if an air–oxygen mix is being used in the anesthetic. A pulmonary artery catheter can detect pulmonary hypertension resulting from reflex vasoconstriction and direct obstruction in the presence of venous air embolism, but because of its invasiveness, it is only recommended when a strong second indication is present.

The use of a right atrial catheter should be considered in any situation when the risk of venous air embolism is high. Traditionally, the tip of the catheter is guided to a position near the sinoatrial node by electrocardiographic guidance, although fluoroscopic placement is now frequently used as a primary or adjunctive technique. The catheter is flushed with $NaHCO_3$, and the right arm lead is attached to a conductive connector placed on the line. The catheter should then be advanced into the right ventricle, which can be detected by transducing the pressure waveform. It should then be drawn back until the P wave on the catheter lead is biphasic (midatrium), and then back further to the point at which the P wave and QRS complex are of equal amplitude. The catheter is then pulled back another centimeter and secured. The right atrial catheter can confirm the presence of venous air embolism through the aspiration of air, but its principal utility is therapeutic: It enables significant volumes of air to be rapidly extracted from the right atrium, thus breaking the "air lock" that causes the loss of cardiac output.

Jadik S, Wissing H, Friedrich K, et al. A standardized protocol for the prevention of clinically relevant venous air embolism during neurosurgical interventions in the semisitting position. *Neurosurgery*. 2009;64:533–538.

Schubert A, Deogaonkar A, Drummond JC. Precordial Doppler probe placement for optimal detection of venous air embolism during craniotomy. *Anesth Analg.* 2006;102:1543–1547.

C.14. Are there any measures you can take to prevent venous air embolism?

The most effective prevention of venous air embolism derives from the surgical technique and the surgeon's tolerance of lower head positions. The anesthesiologist can contribute by ensuring adequate hydration (increasing the height of the venous column) and by avoiding drugs that dilate the venous capacitance vessels, such as nitroglycerin. Positive end-expiratory pressure does not reduce the incidence of venous air embolism, but it does impair surgical conditions through reducing venous return and increase the chance of a paradoxical air embolus in a patient with a patent foramen ovale. Therefore, it should not be used in craniotomies unless there is a strong rationale based on respiratory pathology. The release of positive end-expiratory pressure presents a period of elevated risk of venous air embolism.

Considerable controversy remains over the use of N_2O in the sitting position and other circumstances in which there is a high risk of venous air embolism. The controversy extends to the effect of N_2O on pneumocephalus; studies have shown conflicting results on changes in the size of the gas collection. No study has demonstrated an effect of N_2O on venous air embolism. When these controversies combined with the possible deleterious effects of N_2O on neuroprotection outlined earlier, we see no role for N_2O in posterior fossa craniotomy given the availability of viable alternatives in anesthetic management.

Giebler R, Kollenberg B, Pohlen G, et al. Effect of positive end-expiratory pressure on the incidence of venous air embolism and on the cardiovascular response to the sitting position during neurosurgery. *Br J Anaesth.* 1998;80:30–35.

Losasso TJ, Muzzi DA, Dietz NM, et al. Fifty percent nitrous oxide does not increase the risk of venous air embolism in neurosurgical patients operated upon in the sitting position. *Anesthesiology.* 1992;77:21–30.

Pasternak JJ, Lanier WL. Is nitrous oxide use appropriate in neurosurgical and neurologically at-risk patients? *Curr Opin Anaesthesiol.* 2010;23:544–550.

Schmitt HJ, Hemmerling TM. Venous air emboli occur during release of positive end-expiratory pressure and repositioning after sitting position surgery. *Anesth Analg.* 2002;94:400–403.

C.15. During the procedure, the precordial Doppler becomes loud and turbulent. The end-tidal CO_2 ($ETco_2$) drops from 31 mm Hg to 13 mm Hg, and the systemic pressure from 121/63 mm Hg to 64/32 mm Hg. What is your assessment and management plan?

This is a classic presentation of venous air embolism. Immediately inform the surgeon and institute 100% oxygen. The surgeon should flood the field with saline and urgently prepare the field for lowering the head (e.g., placement of a protective drape). Where possible, an assistant should reach under the drapes and apply pressure to the jugular veins to prevent further entrainment (but not enough to occlude carotid flow), although this should be only a transient measure. Intravenous fluids should be opened to full flow. The head should then be lowered to a level below the heart, or as much as is possible. The left lateral decubitus position has been advocated, but is probably of little benefit. If a right atrial catheter is in place, air should be aspirated. Other management is supportive.

If the venous air embolism is detected early, the episode will usually resolve. It is almost always appropriate to resume and complete the surgery, although placement of additional monitors before resumption might be warranted. Undetected, massive, or prolonged entrainment of air can lead to cardiac arrest. If cardiac arrest is present or imminent, and the patient is in a prone or semiprone position, the anesthesiologist must prepare the surgeon and others in the room for an emergent move to the supine position to enable resuscitation. For this reason, a stretcher must always be available outside the operating room when patients are in the prone position.

Kerr RH, Applegate RL 2nd. Accurate placement of the right atrial air aspiration catheter: a descriptive study and prospective trial of intravascular electrocardiography. *Anesth Analg.* 2006;103:435–438.

Mirski MA, Lele AV, Fitzsimmons L, et al. Diagnosis and treatment of vascular air embolism. *Anesthesiology.* 2007;106:164–177.

C.16. What is your approach to emergence? What if the patient does not wake up?

Providing an early neurologic assessment is one of the most valuable contributions of the anesthesiologist to outcome in neurosurgical patients. Therefore, it is imperative to have patients emerge quickly, even when surgery has been prolonged. At the same time, the emergence from anesthesia incurs substantial changes in pressure, $Paco_2$, CBF, and autonomic activity and therefore must be carefully planned. Transitioning from hyperventilation should be gradual in order to prevent rebound acidosis. Adrenergic blocking agents should be administered to attenuate the sympathetic effects often seen during and following emergence in these patients. Nicardipine can be considered if the patient exhibits refractory hypertension or hyperreactivity. Reversal of neuromuscular block should be carefully titrated to avoid autonomic instability, with care taken to ensure that the patient does not move while the head is fixed in pins. Antiemetic therapy should be aggressive, because the elevation in ICP caused by retching and vomiting are particularly undesirable in craniotomy patients.

Coughing or "bucking" during emergence causes dramatic spikes in ICP and must be avoided. Several approaches can be used to avoid this, including the use of intravenous lidocaine, an opioid-based anesthetic, or a deep extubation. In the case of a deep extubation, it must be kept in mind that there is always a risk that an intraoperative neurologic event might cause delayed or failed emergence. A strategy of converting the final phase of the anesthetic to a high-dose remifentanil 0.3 to 0.4 μg/kg/min infusion can be highly effective and enables the volatile agent to be eliminated without the patient reacting. After return of ventilation and cognition, remifentanil infusion is stopped and the patient is extubated.

A failure to emerge can represent a neurologic event resulting from the surgery, such as an intracranial bleed, vessel occlusion, embolic event, or seizure. In such cases, the time to diagnosis is a critical determinant of outcome. The anesthesiologist must be able to state with confidence that the delayed emergence is unlikely to be pharmacologic. The usual approach is to immediately perform a CT scan; the operating room should be left available in the event that an emergent return is required.

In some posterior fossa procedures—especially when near the brainstem—postoperative edema can lead to an anticipated worsening of neurologic status before subsequent improvement on the first or second postoperative day, thereby necessitating prolonged intubation. In these cases, the patient can be awakened at the conclusion of the surgery and once a neurologic assessment is obtained, resedated for transport to the ICU. A remifentanil infusion of approximately 0.1 μg/kg/min usually enables an intubated patient to perform a cognitive examination and tolerate the presence of the endotracheal tube.

Bilotta F, Lam AM, Doronzio A, et al. Esmolol blunts postoperative hemodynamic changes after propofol-remifentanil total intravenous fast-track neuroanesthesia for intracranial surgery. *J Clin Anesth.* 2008;20:426–430.

Lauta E, Abbinante C, Del Gaudio A, et al. Emergence times are similar with sevoflurane and total intravenous anesthesia: results of a multicenter RCT of patients scheduled for elective supratentorial craniotomy. *J Neurosurg Anesthesiol.* 2010;22:110–118.

Schubert A, Mascha EJ, Bloomfield EL, et al. Effect of cranial surgery and brain tumor size on emergence from anesthesia. *Anesthesiology.* 1996;85:513–21.

D. Postoperative Management

D.1. What postoperative complications are of greatest concern? What level of monitoring is required?

Part of the neurologic assessment conducted immediately on emergence should be an evaluation of the lower cranial nerves. Damage to the nerves or to nuclei can result in difficulty swallowing and protecting the airway. The principal concern is the development of edema or hematoma causing compression of the brainstem or midbrain structures. The brainstem sits in an anatomic location with very low compliance; even small degrees of edema that would be well tolerated following supratentorial procedures can lead to catastrophic neurologic compromise. It is critical to appreciate that edema and hematoma can develop over the course of several hours following the procedure; a patient who had a satisfactory emergence might deteriorate neurologically in the middle of the night. In certain circumstances, the risk of postoperative edema is so high that the patient is left intubated prophylactically, as discussed earlier. Deterioration cannot always be anticipated, and these patients should be initially monitored in an intensive care setting in all cases.

Dubey A, Sung WS, Shaya M, et al. Complications of posterior cranial fossa surgery: an institutional experience of 500 patients. *Surg Neurol.* 2009;72:369–375.

Suri A, Mahapatra AK, Bithal P. Seizures following posterior fossa surgery. *Br J Neurosurg.* 1998;12:41–44.

CHAPTER 17

Carotid Endarterectomy

Maria Bustillo and Cynthia A. Lien

AN 85-YEAR-OLD WOMAN

is scheduled for a left carotid endarterectomy for asymptomatic left carotid stenosis. She has 90% occlusion of her left carotid artery and 60% occlusion of the right carotid artery. Her past medical history is remarkable for hypertension, insulin-dependent diabetes mellitus, and coronary artery disease. She had coronary artery bypass surgery 4 years ago. Her blood pressure is 170/80 mm Hg and her pulse is 59 beats per minute and regular.

A. Medical Disease and Differential Diagnosis

1. What are the presenting symptoms of carotid stenosis?
2. What is the prevalence of carotid artery disease?
3. What is the natural course of carotid artery disease?
4. Discuss diabetes mellitus as a risk factor for carotid endarterectomy.
5. What are the indications for surgical intervention in the management of carotid atherosclerotic disease?
6. Discuss the anatomy of the cerebral vasculature, including the carotid artery and the circle of Willis.
7. Discuss cerebral perfusion in the presence of carotid artery disease.
8. Discuss the different surgical approaches to carotid revascularization.
9. What is normal cerebral blood flow (CBF)?
10. What is critically low CBF as measured by the electroencephalogram (EEG)?
11. What is cerebral autoregulation?
12. How does $Paco_2$ affect CBF?
13. What are the principal determinants of CBF?
14. What is meant by the term *luxury perfusion*?
15. What is meant by the term *intracerebral steal*?
16. What is "inverse steal" or the "Robin Hood" syndrome?

B. Preoperative Evaluation and Preparation

1. What will you be looking for in your preoperative evaluation of this patient?
2. Is this patient's blood pressure too high for elective surgery?
3. What laboratory data are required preoperatively?
4. Will you premedicate this patient?

C. Intraoperative Management

1. How will you monitor this patient?
2. How will you know that the patient's cerebral perfusion is adequate during surgery?
3. Discuss the differences and relative advantages and disadvantages of the unprocessed EEG and the processed EEG.
4. How will you measure CBF intraoperatively? What are the relative advantages and disadvantages of each technique? How much CBF is considered adequate?
5. Does internal carotid stump pressure accurately reflect cerebral perfusion?
6. Discuss somatosensory evoked potentials (SSEPs) as a monitor of CBF during carotid endarterectomy.
7. Describe the role of the transcranial Doppler as a monitor of cerebral perfusion during carotid endarterectomy.
8. What type of anesthesia will you choose for this patient?
9. How will you induce and maintain general anesthesia in this patient?
10. How would you proceed if the patient were to receive regional anesthesia?
11. Discuss the effects of anesthetics on CBF.
12. Discuss the protective effects of anesthetic agents on cerebral function.
13. How will you manage this patient's ventilation under general anesthesia?
14. How will you manage this patient's blood pressure intraoperatively?
15. Discuss reperfusion injury following carotid endarterectomy and carotid artery stenting.
16. What intravenous fluids will you give this patient intraoperatively?

D. Postoperative Management

1. The patient does not "wake up" from general anesthesia. Why?
2. Postoperatively, the patient's blood pressure is 170/96 mm Hg. Will you treat this?
3. What immediate postoperative complications might you expect?
4. Discuss postoperative neurocognitive dysfunction following uncomplicated carotid endarterectomy.

A. Medical Disease and Differential Diagnosis

A.1. What are the presenting symptoms of carotid stenosis?

Carotid disease may manifest as only an asymptomatic bruit. It can also present, though, with amaurosis fugax, a transient ischemic attack (TIA), or a cerebrovascular accident. Amaurosis fugax is a temporary monocular blindness caused by a TIA of the retina. It is an indication of an evolving arterial thrombus in the internal carotid artery, which is the main blood supply to the optic nerve and retina through the ophthalmic artery. The symptoms of amaurosis fugax, which have been described as a shade descending over one eye, often last less than 10 minutes, and are ipsilateral to the evolving and symptomatic vascular disease.

Other manifestations of symptomatic carotid artery disease include episodes of paresthesias, clumsiness, or difficulties with speech that resolve spontaneously over a short period.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1117–1122.

Brunicardi FC, Andersen DK, Billian TR, et al., eds. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:931–1004

Fauci AS, Braunwald E, Kasper DL, et al., eds. *Harrison's Principles of Internal Medicine*. 17th ed. New York: McGraw-Hill; 2008:2517–2518

A.2. What is the prevalence of carotid artery disease?

Carotid artery disease is a manifestation of generalized arteriosclerosis. A review of data contained in the medical records of Mayo Medical Center shows the incidence of TIA to be 31 per 100,000 people in Rochester, Minnesota. The incidence increases with age. Its incidence is 1 per 100,000 in people younger than 45 years old and increases to 293 per 100,000 in people 75 years and older. In patients with an asymptomatic carotid stenosis of less than 75%, the risk of developing a TIA is 1% to 2% per year.

Similar rates have been reported in the former Union of Soviet Socialist Republics. Stroke remains the third most common cause of death in the United States. Heart disease and cancer are the first and second leading causes of death.

Meyer FB, ed. *Sundt's Occlusive Cerebrovascular Disease*. 2nd ed. Philadelphia: WB Saunders; 1994:60.

Minino AM, Smith BL. *Deaths: Preliminary Data from 2000: National Vital Statistics Reports*. Hyattsville, MD: National Center for Health Statistics; 2000;49:1.

Wilke HJ, Ellis JE, McKinsey JF. Carotid endarterectomy: perioperative and anesthetic considerations. *J Cardiothorac Vasc Anesth*. 1996;10:928.

A.3. What is the natural course of carotid artery disease?

In carotid artery disease, atherosclerotic plaques develop at the lateral aspect of the bifurcation of the carotid artery. The severity of the process parallels that in other major vessels. Thrombosis is most likely to occur where the plaque narrows the lumen to the greatest degree. Thromboembolic stroke accounts for the greatest percentage of cerebrovascular accidents.

Sixty percent of thrombotic strokes are preceded by one or more TIAs. Most frequently one or two TIAs will occur before the final stroke and each will last less than 10 minutes. In more than 25% of cases, a complete stroke will follow a TIA within 1 month. In approximately 30% of cases, TIA do not precede a stroke. Embolic and hemorrhagic strokes are rarely preceded by TIAs.

In a patient population in Rochester, Minnesota, the 50% survival time after the first TIA was 7 to 8 years. The highest mortality rate was in the first 2 years following a TIA. However, 2 years following a TIA, the mortality rate stabilized at 1.5 times that of the general population.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1117–1122.

Fields WS, Maslenikov V, Meyer JS, et al. Joint study of extracranial arterial occlusion. Part V. Progress report of prognosis following surgery or nonsurgical treatment for cerebral ischemic attacks and cervical carotid artery lesions. *JAMA*. 1970;211:1993.

Matsumoto N, Whisnant JP, Kurland LT, et al. Natural history of stroke in Rochester Minnesota, 1955 through 1969: an extension of a previous study, 1945 through 1954. *Stroke*. 1973;4:20.

Meyer FB, ed. *Sundt's Occlusive Cerebrovascular Disease*. 2nd ed. Philadelphia: WB Saunders; 1994:60.

A.4. Discuss diabetes mellitus as a risk factor for carotid endarterectomy.

Diabetes is a major risk factor for stroke. When matched for associated risk factors, symptomatic cerebrovascular disease is more common in patients who have diabetes mellitus than in those who do not have diabetes. The risk of stroke is at least 2.5 times greater in diabetic than in nondiabetic patients. Additionally, mortality and the severity of stroke are greater in patients with diabetes.

In a study from 1992 to 1995, 732 carotid endarterectomies were performed in diabetic and nondiabetic patients. A greater percentage of patients with diabetes, compared to patients without diabetes, who underwent carotid endarterectomy were women. Patients with diabetes were younger at presentation than nondiabetic patients and were more likely to have history of coronary artery disease. This may contribute to the higher incidence of postoperative cardiac morbidity in diabetic patients. By itself, diabetes mellitus is not a risk factor for postoperative cardiac morbidity in patients who undergo carotid surgery.

Diabetes mellitus and obesity are considered independent risk factors for neurocognitive decline after carotid endarectomy.

Akabari CM, Pomposelli FB, Gibbons GW, et al. Diabetes mellitus: a risk factor for carotid endarterectomy? *J Vasc Surg*. 1997;24:1070.

Heyer EJ, Wilson DA, Sahlein DH, et al. APOE-ε 4 predisposes to cognitive dysfunction following uncomplicated carotid endarterectomy. *Neurology*. 2005;65:1–5.

Kannel WB, McGee DL. Diabetes and cardiovascular disease the Framingham study. *JAMA*. 1979;241:235–238.

Stokes J, Kannel WB, Wolf PA, et al. The relative importance of selected risk factors for various manifestations of cardiovascular disease among men and women from 35 to 64 years old: 30 years of follow-up in the Framingham study. *Circulation*. 1987;75:65.

A.5. What are the indications for surgical intervention in the management of carotid atherosclerotic disease?

Currently in the United States, there are more than 700,000 new strokes per year and it is estimated that 20% to 30% are due to carotid atherosclerotic disease.

Accepted indications for surgery currently include the following:

- TIAs with angiographic evidence of stenosis
- Reversible ischemic neurologic deficits with greater than 70% stenosis of the vessel wall or an ulcerated plaque, with or without stenosis
- An unstable neurologic status that persists despite anticoagulation.

In the North American Symptomatic Carotid Endarterectomy Trial, carotid endarterectomy decreased the risk of an ipsilateral stroke from 26% to 9%, yielding an absolute risk reduction of 65%. Similar results were obtained in the European Carotid Surgery Trial, which demonstrated a 39% risk reduction, and the Veterans Affairs Cooperative Trial, which demonstrated a 60% risk reduction from a severe stroke with surgical versus medical therapy.

A multicenter study of 1,662 asymptomatic patients (asymptomatic carotid atherosclerosis study) with carotid stenosis of 60% or more as determined by Doppler studies, demonstrated that patients undergoing carotid endarterectomy in addition to medical therapy had a 53% reduction in aggregate risk for stroke or death compared to patients receiving only medical therapy. Additional outcome studies are warranted before carotid endarterectomy is recommended as a routine therapy for asymptomatic carotid artery disease.

Asymptomatic Carotid Atherosclerosis Study Group; Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. Endarterectomy for asymptomatic carotid artery stenosis. *JAMA*. 1995;273:1421.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott, Williams & Wilkins; 2009:1117–1122.

Barnett HJM, Meldrum HE, Eliasziw M. The dilemma of surgical treatment for patients with asymptomatic carotid disease. *Ann Intern Med*. 1995;123:723–725.

Brunicardi FC, Andersen DK, Billian TR, et al., eds. *Schwartz's Principles of Surgery*. 8th ed. New York: McGraw-Hill; 2005:780–788.

The CASANOVA Study Group. Carotid surgery versus medical therapy in asymptomatic carotid stenosis. *Stroke*. 1991;22:1229–1235.

European Carotid Surgery Trialists Collaborative Group. MRC European Carotid Surgery Trial: interim results for symptomatic patients with severe (70–90%) or with mild (0–29%) carotid stenosis. *Lancet*. 1991;337:1235–1243.

Hobson RW, Weiss DG, Fields WS, et al. Efficacy of carotid endarterectomy for asymptomatic carotid stenosis. The Veterans Affairs Cooperative Study Group. *N Engl J Med*. 1993;328:221–227.

Mayberg MR, Wilson SE, Yatsu F, et al. The Veterans Affair Cooperative Studies Program 309 Trialist Group. Carotid endarterectomy and prevention of cerebral ischemia is symptomatic carotid stenosis. *JAMA*. 1991;226:3289–3294.

Mayo Asymptomatic Carotid Endarterectomy Study Group. Results of a randomized controlled trial of carotid endarterectomy of asymptomatic carotid stenosis. *Mayo Clin Proc*. 1992;67:513–518.

North American Symptomatic Carotid Endarterectomy Trial Collaborators. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. *N Engl J Med*. 1991;325:445–453.

A.6. Discuss the anatomy of the cerebral vasculature, including the carotid artery and the circle of Willis.

The common carotid arteries originate in the thorax. The right common carotid artery originates at the bifurcation of the brachiocephalic trunk, and the left originates from the aortic arch. In the neck, the common carotid arteries travel within the carotid sheath. At the level of the thyroid cartilage, each common carotid artery bifurcates into internal and external carotid arteries.

Branches of the external carotid artery include the superior thyroid, lingual, facial, ascending pharyngeal, occipital, and posterior auricular arteries.

The internal carotid artery passes through the neck without branching to enter the middle cranial fossa. It enters the middle cranial fossa through the carotid canal of the temporal bone, adjacent to the sphenoid bone. It supplies the hypophysis cerebri, the orbit, and the major portion of the supratentorial region of the brain. The cerebral arteries are derived from the internal carotid and vertebral arteries. The anastomosis they form at the base of the brain is known as the *circle of Willis*. The two anterior cerebral arteries form the circle anteriorly. They are connected through the anterior communicating artery. The two posterior cerebral arteries form the circle posteriorly, which then ends at the junction of the basilar artery. The posterior cerebral arteries are connected to the internal carotid arteries by the two posterior communicating

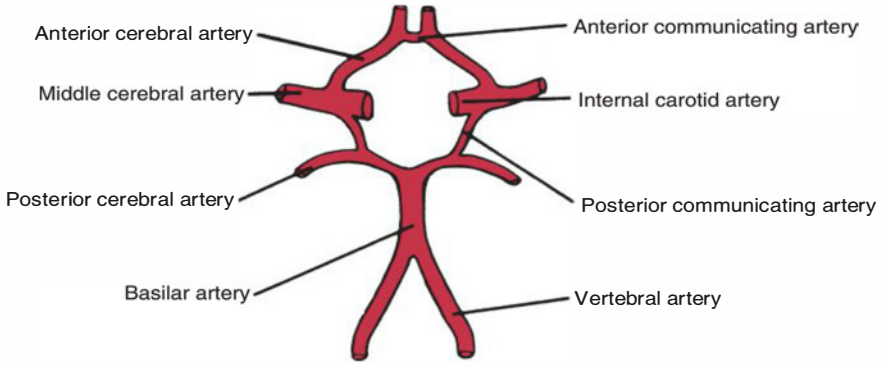

Figure 17.1 Arterial circle of Willis.

arteries (Fig. 17.1). The middle cerebral artery primarily supplies the lateral surface of each cerebral hemisphere. The anterior cerebral and posterior cerebral arteries supply the medial and inferior surfaces of the cerebral hemisphere.

Hemmings HC, Hopkins PM, eds. *Foundations of Anesthesia Basic Science for Clinical Practice*. 2nd ed. Philadelphia: Elsevier; 2006:245.

Moore KL. *Clinically Oriented Anatomy*. 5th ed. Baltimore: Lippincott Williams & Wilkins; 2006;930–931.

A.7. Discuss cerebral perfusion in the presence of carotid artery disease.

Autoregulation is assumed to be lost in underperfused areas of the brain. Vascular regions subjected to chronic hypoperfusion and relative ischemia are maximally vasodilated and unresponsive to factors that induce vasoconstriction in normally reactive vascular beds. Therefore, in patients with carotid artery disease, blood flow through ischemic regions is passive and dependent on systemic blood pressure. For this reason, hypotension is best avoided in the period before restoration of unobstructed CBF.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1117–1122.

Ehrenfeld WK, Hamilton FN, Larson CP, et al. Effect of CO_2 and systemic hypertension on downstream cerebral arterial pressure during carotid endarterectomy. *Surgery*. 1970;67:87–96.

Fourcade HE, Larson CP, Ehrenfeld WK, et al. The effects of CO_2 and systemic hypertension on cerebral perfusion pressure during carotid endarterectomy. *Anesthesiology*. 1970;33:383–390.

A.8. Discuss the different surgical approaches to carotid revascularization.

Carotid endarterectomy involves the removal of atheromatous plaque from the vessel lumen through a fairly standardized surgical procedure. This involves occluding the common, external, and internal carotid arteries, isolating the diseased segment, opening the vessel wall, and removing the plaque. The vessel is then closed. If the

remaining intima is too thin, the vessel is closed with a vein graft or a synthetic (Dacron) patch. The use of a shunt during the period of carotid cross-clamping depends on whether evidence of cerebral ischemia becomes apparent with cross-clamping of the carotid artery. Variations in shunt usage exist because there is little evidence that one therapy is superior to the others. Placement of a shunt allows hemispheric CBF to be maintained during cross-clamping and may be especially advantageous when the endarterectomy is expected to be complex and require a long time.

On the other hand, shunt usage is not without its problems. It may make the surgery technically more difficult. Technical problems with shunts include plaque or air embolism, kinking of the shunt, shunt occlusion on the side of the vessel wall, and injury to the distal internal carotid artery. The use of a shunt does not guarantee adequate CBF nor prevent thromboembolic strokes.

Another intervention to treat carotid stenosis is percutaneous transluminal angioplasty and stenting by interventional radiologists. Advantages to endovascular techniques include avoidance of surgical incision; minimal anesthetic requirements; avoidance of minor complications associated with endarterectomy, including cranial nerve injury and wound infections; shorter duration of induced carotid occlusion by the balloon catheter than with surgical clamping of the carotid artery; and lower hospital costs for shorter hospital and intensive care unit stays.

Clinical trials comparing carotid endarterectomy with angioplasty have been done. Early trials were stopped prematurely because of significantly worse outcomes among patients treated with angioplasty.

The Carotid Revascularization Using Endarterectomy or Stenting Systems phase I study was a multicenter, prospective, nonrandomized trial designed to address the question of whether carotid artery stenting with cerebral protection was comparable to carotid endarterectomy in patients with symptomatic and asymptomatic carotid stenosis. A total of 397 patients (254 carotid artery surgery and 143 carotid artery stenting) were enrolled in the study: 32% were symptomatic and 68% were asymptomatic. There were no significant differences in patient demographics, symptoms, or surgical risk profiles between groups at baseline. There were no significant differences in combined death or stroke rates at 30 days or 1 year after treatment. Similarly, there was no significant difference in the combined end point of death, stroke, or myocardial infarction at 30 days or 1 year between the two groups. There were also no significant differences between the treatment groups in terms of the secondary end points of residual stenosis, restenosis, repeat angiography, carotid revascularization, or change in quality of life. The results of the Carotid Revascularization Using Endarterectomy or Stenting Systems phase I study suggest that the 30-day and 1-year risk for death, stroke, or myocardial infarction with coronary artery stenting is equivalent to that with carotid endarectomy in symptomatic and asymptomatic patients with carotid stenosis.

The Carotid and Vertebral Artery Transluminal Angioplasty Study was the first randomized trial comparing carotid endarterectomy to angioplasty. A total of 504 patients with symptomatic stenosis and more than 50% occlusion were randomly assigned to either endovascular treatment or surgery. Within 30 days of treatment, there were more minor strokes lasting less than 7 days in the endovascular group. The numbers of more major strokes or death were the same regardless of treatment group. None of the differences in stroke outcome measures was significant. The study results suggest that angioplasty and carotid endarterectomy are equally effective in preventing stroke. Additionally, disabling stroke and death rates were the same after surgery and stenting. The study, though, was underpowered.

The Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy (SAPPHIRE) trial is the most recently published study comparing carotid artery stenting and carotid endarterectomy. In this trial, 334 high-risk patients with carotid stenosis were randomized to either stenting or surgery (167 each group). Randomization to stenting with embolic protection was found to not be inferior to carotid endarterectomy for reducing the primary clinical end points (composite of

death, stroke, or myocardial infarction within 30 days, and death or ipsilateral stroke between 31 and 365 days). There was a strong trend toward reduction of the primary end point with stenting and fewer required carotid revascularizations at 1 year.

Health-related quality of life outcomes were assessed at baseline, 2 weeks following treatment, and during an additional follow-up visits at 1, 2, 6, and 12 months. Patients treated with stenting had significant health benefits during the early recovery period when compared to those treated with surgery. The duration of any benefit, though, was limited to the first 2 weeks of the postoperative period, and all other measures of disease-specific health status, as well as general health and physical function, were similar at 1, 2, 6, and 12 months.

Although the results of the SAPPHIRE trial demonstrated similar results whether carotid artery stenosis was treated with stenting or surgery when stenting was done by surgeons experienced in the technique, the findings of another report, also published in 2010, demonstrated that physicians in a formalized training program with varied individual levels of experience could have results similar to those obtained in the SAPPHIRE trial.

The CaRESS Steering Committee. Carotid Revascularization Using Endarterectomy or Stenting Systems (CaRESS) phase I clinical trial: 1-year results. *J Vasc Surg*. 2005;42:213–219.

The CAVATAS Investigators. Endovascular versus surgical treatment in patients with carotid stenosis in the Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS): a randomized trial. *Lancet*. 2001;357:1729.

Ederle J, Bonati LH, Dobson J, et al. Endovascular treatment with angioplasty or stenting versus endarterectomy in patient with carotid artery stenosis in the Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS): long-term follow-up of a randomized trial. *Lancet Neurol*. 2009;8:898–907.

Schreiber TL, Strickman N, Davis T, et al. Carotid artery stenting with emboli protection surveillance study: outcomes at 1 year. *J Am Coll Cardiol*. 2010;56:49–57.

Stolker JM, Mahoney EM, Safley DM, et al. Health-related quality of life following carotid stenting versus endarterectomy: results from the SAPPHIRE (Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy) trial. *JACC Cardiovasc Interv*. 2010;3:515–523.

Sundt TM, Houser OW, Sharbrough FW, et al. Carotid endarterectomy: results, complications and monitoring techniques. *Adv Neurol*. 1977;16:97–119.

Thompson JE, Talkington CM. Carotid endarterectomy. *Ann Surg*. 1978;184:1–15.

Wylie EJ, Stoney RJ, Ehrenfeld WK, eds. *Manual of Vascular Surgery*. Vol. I. *Comprehensive Manuals of Surgical Specialties Series*. New York: Springer-Verlag; 1980:49–84.

Wilke HJ, Ellis JE, McKinsey JF. Carotid endarterectomy: perioperative and anesthetic considerations. *J Cardiothorac Vasc Anesth*. 1996;10:928–949.

Yadav JS, Wholey MH, Kuntz RE, et al. Protected carotid-artery stenting versus endarterectomy in high risk patients. *N Engl J Med*. 2004;351:1493–1501.

A.9. What is normal cerebral blood flow (CBF)?

Normal CBF is approximately 50 mL/100 g/min for the entire brain. Blood flow is approximately four times higher in gray matter than it is in white matter, with the flows being 80 and 20 mL/100 g/min, respectively.

Hemmings HC, Hopkins PM, eds. *Foundations of Anesthesia Basic Science for Clinical Practice*. 2nd ed. Philadelphia: Elsevier Science; 2006:248–249.

Kety SS, Schmidt CF. The nitrous oxide method for the quantitative determination of cerebral blood flow in man: theory, procedure and normal values. *J Clin Invest*. 1948;27:476–483.

Lassen NA, Munch O. The cerebral blood flow in man determined by the use of radioactive krypton. *Acta Physiol Scand.* 1955;33:30–49.

A.10. What is critically low CBF as measured by the electroencephalogram (EEG)?

Assuming a normal temperature and hematocrit, 100 mL of blood contains approximately 20 mL of oxygen. A normal global CBF flow of 50 mL/100 g/min delivers oxygen to the brain at a rate of 10 mL/100 g/min. This is in excess of the high metabolic requirements of the brain for oxygen (3 to 5 mL/100 g/min), which affords a relative margin of safety. The CBF at which ischemia becomes apparent in the EEG is approximately 20 ml/100 g/min. Changes on EEG may be delayed for up to 150 seconds following the onset of ischemia. It is impossible to define the specific changes that represent irreversible ischemia. In the setting of an isoelectric EEG, oxygen delivery to the brain may be adequate to keep the neurons alive but may provide insufficient energy for them to function.

The development of cerebral infarction depends on both the degree and duration of ischemia. Jones showed in an animal model of reversible ischemia that with CBF of 18 to 23 mL/100 g/min, animals would recover from impaired neurologic function when blood flow was returned to normal levels, regardless of the duration of the ischemic period. Infarction development at lower flows depends on both the degree of regional CBF reduction and the duration of ischemia. Neurons that are nonfunctional but will recover fully with restoration of adequate flow are said to be in an ischemic penumbra. Neuronal destruction occurs with CBF less than 10 mL/100 g/min.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia.* 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1117–1122.

Boysen G, Engell HC, Pitolese GR, et al. On the critical level of cerebral blood flow in man with particular reference to carotid surgery. *Circulation.* 1974;49:1023.

Jones TH, Morawetz RB, Crowell RM, et al. Threshold of focal cerebral ischemia in awake monkeys. *J Neurosurg.* 1981;54:773–782.

Levy WJ. Intraoperative EEG patterns: implications for EEG monitoring. *Anesthesiology.* 1984;60:430–434.

Trojaborg W, Boysen G. Relation between EEG, regional cerebral blood flow and internal carotid artery pressure during carotid endarterectomy. *Electroencephalogr Clin Neurophysiol.* 1973;34:61–69.

A.11. What is cerebral autoregulation?

Cerebral autoregulation is the tendency of the brain to match cerebral metabolic oxygen requirements with oxygen delivery in spite of variations in blood pressure. In normotensive individuals, CBF is constant between mean arterial pressures of 50 and 150 mm Hg. What this means is that cerebrovascular resistance increases, through vasoconstriction, as mean arterial pressure increases from 50 to 150 mm Hg. At pressures greater than 150 mm Hg, the cerebral vasculature is maximally vasoconstricted and CBF increases with increasing pressure. At pressures less than 50 mm Hg, cerebral vessels are maximally vasodilated, so that CBF decreases as mean arterial pressure falls.

In hypertensive patients, the upper and lower limits of the autoregulatory curve are shifted to the right, to higher pressures (Fig. 17.2). What this means is that a mean arterial pressure of 60 mm Hg, which would be well tolerated in a normotensive individual, may actually be below the lower limit of autoregulation in the hypertensive individual, resulting in cerebral hypoperfusion. Conversely, hypertensive patients tolerate marked increases in mean arterial pressure much better than their normotensive counterparts. In treated hypertensive patients, the limits of autoregulation are shifted with time toward normal.

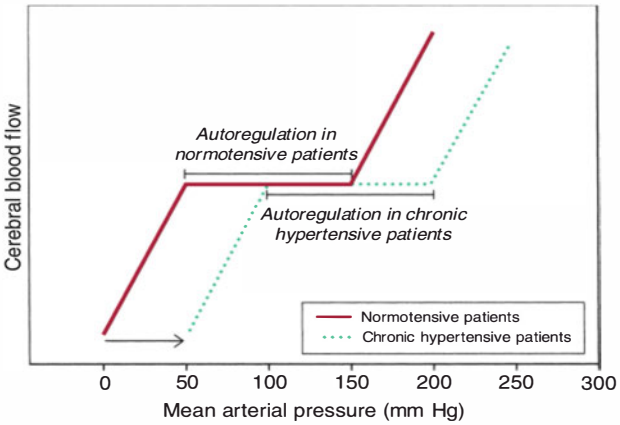

Figure 17.2 Cerebral autoregulatory curves in normotensive and chronic hypertensive patients. New autoregulation curve is achieved with chronic hypertension. The curve shifts back to normotensive range once hypertension is well controlled.

Haggendal E, Lofgren J, Nilsson NJ, et al. Effects of varied cerebrospinal fluid pressure on cerebral blood flow in dogs. *Acta Physiol Scand*. 1970;79:262–271.

Hemmings HC, Hopkins PM, eds. *Foundations of Anesthesia Basic Science for Clinical Practice*. 2nd ed. Philadelphia: Elsevier Science; 2006:249–250.

Symon L, Pasztor E, Dorsch NWC, et al. Physiological responses of local areas of the cerebral circulation in experimental primates determined by the method of hydrogen clearance. *Stroke*. 1973;4:632–642.

A.12. How does $Paco_2$ affect CBF?

Hypercarbia results in cerebral vasodilation and hypocarbia in cerebral vasoconstriction. CBF changes approximately 4% for each millimeter of mercury increase or decrease in arterial $Paco_2$ for partial pressures of arterial carbon dioxide between 20 and 80 mm Hg.

Hemmings HC, Hopkins PM, eds. *Foundations of Anesthesia Basic Science for Clinical Practice*. 2nd ed. Philadelphia: Elsevier Science; 2006:249–250.

Skinhoj E, Paulson OB. Carbon dioxide and cerebral circulatory control: evidence of a nonfocal site of action of carbon dioxide on the cerebral circulation. *Arch Neurol*. 1969;20:249–252.

A.13. What are the principal determinants of CBF?

The principal determinants of CBF are nerve cell activity, cerebral perfusion pressure, $Paco_2$, the pH of the extracellular fluid in the brain, Pao_2, and neurogenic influences.

Cottrell JE, Smith DS. *Anesthesia and Neurosurgery*. 4th ed. St. Louis, MO: Mosby; 2001:19–32.

Hemmings HC, Hopkins PM, eds. *Foundations of Anesthesia Basic Science for Clinical Practice*. 2nd ed. Philadelphia: Elsevier Science; 2006:247–250.

A.14. What is meant by the term *luxury perfusion*?

Luxury perfusion is blood flow that is in excess of metabolic need (increased CBF relative to cerebral metabolic rate for oxygen). It is most frequently observed in tissues surrounding tumors or areas of infarction. It has also been described in tissues that have been manipulated during surgery.

Paulson OB. Cerebral apoplexy (stroke): pathogenesis, pathophysiology and therapy as illustrated by regional blood flow measurements in the brain. *Stroke.* 1971;2:327–360.

A.15. What is meant by the term *intracerebral steal*?

Intracerebral steal is a paradoxical response to carbon dioxide in which hypercapnea decreases the blood flow in an ischemic area. It is the consequence of the vasodilatory effect of carbon dioxide on the normally perfused arterioles at the periphery of an ischemic lesion. Because chronically ischemic vascular beds are maximally vasodilated, they cannot dilate further in response to hypercapnea.

Paulson OB. Cerebral apoplexy (stroke): pathogenesis, pathophysiology and their therapy as illustrated by regional blood flow measurements in the brain. *Stroke.* 1971;2:327–360.

A.16. What is "inverse steal" or the "Robin Hood" syndrome?

Inverse steal is the effect of hypocapnea producing increased blood flow to ischemic regions of the brain. Vasoconstriction occurs in adjacent, normal arterioles, thereby causing a local increase in perfusion pressure and augmenting collateral flow to the ischemic, unreactive, maximally vasodilated area of the brain.

Betz E. Cerebral blood flow: its measurement and regulation. *Physiol Rev.* 1972;52:595–630.

B. Preoperative Evaluation and Preparation

B.1. What will you be looking for in your preoperative evaluation of this patient?

Once the presence of a carotid lesion amenable to surgical treatment has been documented through Doppler, angiographic, or oculoplethysmographic studies, the anesthesiologist will be asked to evaluate the patient regarding her readiness for surgery. The anesthesiologist should determine whether other manifestations of generalized arteriosclerosis, such as coronary artery disease, hypertension, and renal disease are present. Evidence of medical conditions associated with arteriosclerosis, such as obesity, diabetes mellitus, and pulmonary disease secondary to cigarette smoking, should be sought. The patient's neurologic status and airway will need to be evaluated.

Because 30% to 50% of patients undergoing carotid endarterectomy have coronary artery disease, evidence of heart disease should be sought in the patient's history. Patients should be specifically asked whether they have angina or have had a myocardial infarction or congestive heart failure. An indication of daily activity level should be obtained. A patient unable to ambulate for distances because of claudication may never develop angina or left ventricular failure. Therefore, more invasive evaluation of the patient's cardiac function may be required. Evidence of cardiac disease should

also be sought on physical examination. This would include heart rate and rhythm, and presence of jugular venous distention, basilar rales on auscultation of the chest, cardiac enlargement as determined by lateral displacement of the point of maximal impulse, and an S_3 gallop.

Based on the Cardiac Risk Stratification for Noncardiac Surgical Procedures by the American Heart Association/American College of Cardiology Task Force on Assessment of Therapeutic Cardiovascular Procedures, carotid endarterectomy is classified as an intermediate-risk procedure with a reported cardiac risk generally less than 5%.

Whether the patient has hypertension should be determined. Hypertension is present in 55% to 80% of patients with carotid artery disease, and its presence would alter intraoperative blood pressure management. Blood pressure should be measured in both arms with the patient in both the supine and the upright positions. A range of acceptable blood pressures readings, in which the patient is free of symptoms of both cardiac and cerebral ischemia, should be determined. This is done, in part, by reviewing the patient's chart and making note of the highest and lowest blood pressures that were measured. Knowing this range allows the anesthesiologist to determine the range of blood pressures that may be tolerated without treatment in the operating room. Raising the blood pressure excessively to improve cerebral perfusion may exacerbate myocardial ischemia, and lowering the blood pressure to reduce the work of the heart may compromise cerebral perfusion, exacerbating cerebral ischemia.

The presence of other disorders associated with vascular disease, such as obesity, diabetes, and cigarette smoking with their sequelae, should be determined. Evidence of other end-organ effects of vascular disease, such as renal dysfunction, should also be sought.

The patient's neurologic status also needs to be evaluated preoperatively. Although it would be preferable to medically optimize the patient with uncontrolled hypertension or untreated metabolic disease, or if possible, delay surgery in the patient with a recent myocardial infarction, the presence of crescendo TIAs may not allow that option.

The patient's airway needs to be assessed for ease of ventilation and intubation. A patient in whom it is difficult to establish ventilation may become hypercarbic during induction, and the increase in $Paco_2$ may have adverse effects on regional CBF. As part of the airway evaluation, the range of motion of the patient's neck that is tolerated without evidence of cerebral ischemia needs to be determined so that relative extremes of extension and lateral rotation of the neck during ventilation, intubation, and finally patient positioning can be avoided. Extreme extension and rotation of the neck may occlude the patient's vertebral artery and contribute to postoperative neurologic deficits.

Asiddao CB, Donegan JH, Whitesell RC, et al. Factors associated with perioperative complications during carotid endarterectomy. *Anesth Analg.* 1982;61:631–637.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia.* 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1117–1122.

Eagle K, Brundage B, Chaitman B, et al. Guidelines for perioperative cardiac evaluation of the noncardiac surgery. A report of the American Heart Association/American College of Cardiology Task Force on assessment of diagnostic and therapeutic cardiovascular procedures. *Circulation.* 1996;93:1278–1317.

B.2. Is this patient's blood pressure too high for elective surgery?

Although hypertension is present in most patients presenting for carotid endarterectomy, its rapid correction is not recommended because this may exacerbate cerebral

ischemia. If this patient had evidence of myocardial ischemia at this blood pressure and was stable from a neurologic standpoint, blood pressure could be gradually decreased with antihypertensive medications.

Normal myocardial and cerebral function need to be preserved. These goals are not necessarily at odds with each other. To decrease myocardial oxygen consumption, one would want to decrease heart rate, blood pressure, and myocardial contractility. In this patient population, decreasing heart rate can decrease myocardial work, whereas cerebral perfusion pressure is maintained with an adequate mean arterial pressure. If a hypertensive patient presents with an unstable neurologic status, it may be necessary to control blood pressure only once the obstruction to CBF has been relieved.

A single blood pressure measurement is of little use in the preoperative assessment of the patient. It is the range of the blood pressures normally tolerated by the patient that will guide perioperative blood pressure management. For example, if a patient's blood pressure is measured at 80/50 mm Hg and at 170/100 mm Hg preoperatively and at these blood pressures, she does not develop any new neurologic deficits or myocardial ischemia, the clinician will be inclined to treat blood pressures only beyond these two extremes.

Because this patient is hypertensive, one can expect that wide swings in her blood pressure will occur while she is receiving anesthesia. The anesthesiologist must be prepared for these fluctuations by having both vasopressors and vasodilators readily available. Variations in blood pressure should be minimized because these have been related to increased cardiac and neurologic morbidity.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1117–1122.

Hamilton WP. Do let the blood pressure drop and do use myocardial depressants? *Anesthesiology*. 1976;45:273–274.

Smith JS, Roizen MF, Cahalan MK, et al. Does anesthetic technique make a difference? Augmentation of systolic blood pressure during carotid endarterectomy: effects of phenylephrine versus light anesthesia and of isoflurane versus halothane on the incidence of myocardial ischemia. *Anesthesiology*. 1988;69:846–855.

B.3. What laboratory data are required preoperatively?

Laboratory tests should be ordered to determine the patient's baseline cardiac, respiratory, and metabolic status.

Hemoglobin and hematocrit levels should be obtained preoperatively because values may be abnormal in a patient with advanced age or renal or pulmonary disease and because significant blood loss may occur intraoperatively.

A urine analysis and data on blood urea nitrogen and creatinine should be obtained to determine the patient's baseline renal status.

An electrocardiogram (ECG) should be examined preoperatively to look for arrhythmias, evidence of ischemia, previous myocardial infarctions, or left ventricular hypertrophy. Where appropriate, the preoperative ECG should be compared with earlier studies to determine whether interval changes have occurred.

A chest radiograph should be examined to look for cardiomegaly, evidence of pulmonary edema, chronic obstructive pulmonary disease, or pneumonia. If the patient has a history of chronic obstructive pulmonary disease, a preoperative arterial blood gas reading should be obtained to identify the patient's baseline $Paco_2$. In patients who are chronically hypercarbic, rapid adjustment to normocarbia intraoperatively will be interpreted by the body as relative hypocarbia. CBF will be reduced accordingly. Management of intraoperative ventilation should be aimed at maintaining the patient's normal arterial carbon dioxide level.

Further preoperative evaluation would be based on the presence of concurrent disease.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*, 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1117–1122.

B.4. Will you premedicate this patient?

Ideally, the patient should present to the operating room calm and awake. Preoperative anxiety should be alleviated in these patients because it can lead to hypertension, which has been associated with adverse neurologic outcome. Increases in heart rate in the anxious patient lead to increased myocardial oxygen consumption and, potentially, ischemia, ventricular dysfunction, and arrhythmias.

Premedication, however, may lead to ventilatory depression, with resultant hypercarbia and alterations in CBF that can exacerbate cerebral ischemia. Sedation can also interfere with the immediate postoperative neurologic assessment of the patient because it may cause delayed awakening from anesthesia. One of the anesthetic goals for carotid endarterectomy under general anesthesia is to have a patient who promptly emerges from anesthesia and is able to cooperate with a basic neurologic evaluation. A patient who is too sedated at the end of surgery is problematic.

To achieve these goals, a thorough and reassuring preoperative visit alone may provide sufficient anxiolysis. The anesthesiologist should explain the preoperative procedure and what can be expected in the postoperative period, answering any questions that the patient has. If pharmacologic premedication is required, a benzodiazepine (e.g., diazepam 5 mg orally, 1 hour preoperatively; or midazolam 1 to 2 mg intravenously) should provide anxiolysis and minimal respiratory depression.

Bailey PL, Andriano KP, Goldman M, et al. Variability of the respiratory response to diazepam. *Anesthesiology*. 1986;64:460–465.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*, 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1117–1122.

Freeman LJ, Nixon PGF, Sallabank P, et al. Psychological stress and silent myocardial ischemia. *Am Heart J*. 1987;114:477–482.

Leigh JM, Walker J, Janaganathan P. Effect of preoperative anaesthetic visit on anxiety. *Br Med J*. 1977;2:987–989.

C. Intraoperative Management

C.1. How will you monitor this patient?

Patients who are about to undergo carotid endarterectomy are managed with routine monitoring of cardiovascular, pulmonary, and metabolic function, including ECG leads II and V_5, noninvasive blood pressure monitor, pulse oximetry, end-tidal capnometry, and esophageal temperature.

An intra-arterial catheter should be used to monitor the patient's blood pressure closely. Its presence will permit immediate identification of blood pressure changes and allow for repetitive sampling of arterial blood gases.

Whether a pulmonary artery catheter is required to monitor the patient's cardiac function would be dictated solely by the patient's preoperative cardiac status. Carotid endarterectomy is not an operation in which large fluid shifts are anticipated. A pulmonary artery catheter should not be required in the patient with normal left ventricular function.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*, 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009;1117–1122.

C.2. How will you know that the patient's cerebral perfusion is adequate during surgery?

In the awake patient undergoing carotid endarterectomy under local anesthesia, repeated neurologic examinations can be done to assess the adequacy of cerebral perfusion.

If the patient receives general anesthesia, cerebral perfusion or function should be monitored. No currently available clinical monitor is as sensitive and specific for cerebral dysfunction as repeated neurologic examinations, and no one monitor is routinely used in all operating rooms. Some monitors have been used to monitor cerebral perfusion or function. These include the electroencephalograph, somatosensory evoked potentials, transcranial Doppler, internal carotid stump pressure, and jugular venous oxygen saturation.

Current interest has considered cerebral oximetry as a monitor because it is noninvasive, continuous, and easy to use. In recent studies, a relative decrease of 20% or greater in regional cerebral oxygen saturation suggested cerebral ischemia. The monitor, though, has a low positive predictive value and low specificity. If used exclusively, it would suggest the need for unnecessary shunting and lead to overshunting of patients.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1117–1122.

Evans WE, Hayes JP, Waltke EA, et al. Optimal cerebral monitoring during carotid endarterectomy: neurologic response under local anesthesia. *J Vasc Surg*. 1985;2:775–777.

Grubhofer G, Plochl W, Skolka M, et al. Comparing Doppler ultrasonography and cerebral oximetry as indicators for shunting in carotid endarterectomy. *Anesth Analg*. 2000;91:1339–1344.

Grundy BL, Sanderson AC, Webster MW, et al. Hemiparesis following carotid endarterectomy: comparison of monitoring methods. *Anesthesiology*. 1981;55:462–466.

Rosenthal D, Stanton PE Jr, Lamis PA. Carotid endarterectomy: the unreliability of intraoperative monitoring having had stroke or reversible ischemic neurological deficit. *Arch Surg*. 1981;116:1569–1575.

Samra SK, Dy EA, Welch K, et al. Evaluation of a cerebral oximeter as a monitor of cerebral ischemia during carotid endarterectomy. *Anesthesiology*. 2000;93:964–970.

C.3. Discuss the differences and relative advantages and disadvantages of the unprocessed EEG and the processed EEG.

The EEG is neither a measure of CBF nor a way to determine whether irreversible neuronal damage has occurred. Rather, it is an indicator that areas of the brain may be at risk for infarction. Changes that occur in the EEG with hypothermia, hypocarbia, hypoxemia, and deep anesthesia mimic those of ischemia. In patients who have had a cerebrovascular accident, the processed EEG does not predict cerebral ischemia.

Problems associated with intraoperative monitoring of the 16-lead EEG have detracted from its popularity. These include difficulty in obtaining a meaningful recording in the electrically noisy environment of the operating room, the bulk of the equipment required, and the need for specially trained personnel for interpretation. The 16-channel EEG is, nevertheless, a sensitive indicator of ischemia.

The processed EEG has eliminated many of the problems associated with the 16-channel EEG. The equipment is generally compact and the data display allows for ease of interpretation. The most commonly used processed encephalogram is the power spectrum analysis. For this analysis, the EEG is studied in short time intervals of 2 to 16 minutes, called *epochs*. Each epoch then is subjected to a fast Fourier transform analysis during which the complex waveform of the unprocessed EEG is broken down into its component sine waves of varying amplitudes and frequencies. The power spectrum is calculated by squaring the amplitude of the individual frequency components. The power spectrum can then be displayed in various graphic forms, two of which are the compressed spectral array and the density modulated spectral array. Data are displayed in these two forms as relative power versus frequency (Fig. 17.3).

It must be remembered that the processed EEG is only as good as the original from which it was obtained. Therefore, meticulous recording techniques are required even when monitoring a processed EEG. During carotid endarterectomy, generally two or four channels of the EEG are monitored to determine right and left symmetry in neuronal activity during interruption of CBF.

Harris EJ, Brown WH, Pavy RN, et al. Continuous electroencephalographic monitoring during carotid artery endarterectomy. *Surgery*. 1978;83:306–312.

Kearse LA, Lopez-Bresnahan M, McPeck K, et al. Preoperative cerebrovascular symptoms and electroencephalographic abnormalities do not predict cerebral ischemia during carotid endarterectomy. *Stroke*. 1995;26:1210–1214.

Levy W, Shapiro HM, Maruchak G, et al. Automated EEG processing for intraoperative monitoring. *Anesthesiology*. 1980;53:223–236.

Rampil IJ, Holzer JA, Quest DO, et al. Prognostic value of computerized EEG analysis during carotid endarterectomy. *Anesth Analg*. 1983;62:186–192.

Sundt TM, Sharbrough FW, Peipgras DG, et al. Correlation of cerebral blood flow and electroencephalographic changes during carotid endarterectomy. *Mayo Clin Proc*. 1981;56:533–543.

C.4. How will you measure CBF intraoperatively? What are the relative advantages and disadvantages of each technique? How much CBF is considered adequate?

Measurement of regional CBF is the single best method for detecting decreases in CBF during general anesthesia. Multiple different ways are used to measure this. These include the Kety-Schmidt method and later modifications on this, the intracarotid injection method, and the inhalation and intravenous techniques.

The Kety-Schmidt method, as originally described, involved 10 to 16 minutes of inhalation of 15% nitrous oxide. During this period, equilibration would occur among arterial, venous, and tissue concentrations of nitrous oxide. Blood samples would intermittently be taken from a peripheral artery and the jugular bulb to determine tracer concentration. The amount of tracer taken up by the brain in a certain period is equivalent to the amount delivered to the brain in the arterial blood supply minus that recovered in the cerebral venous blood in the same period. If it is assumed that the brain concentration of the tracer is proportional to the tracer concentrations in the cerebral venous blood, global CBF can be determined with knowledge of the blood brain partition coefficient for the tracer used.

Later modifications of this technique employ the radioactive tracers krypton-85 (^{85}Kr) or xenon-133 (^{133}Xe). CBF, as measured using the Kety-Schmidt method and its modifications, may be overestimated in the case of low perfusion states in which brain and venous blood may not equilibrate. One cannot measure regional CBF using these techniques because jugular venous blood is a mixed venous sample with varying amounts of contamination from the contralateral hemisphere.

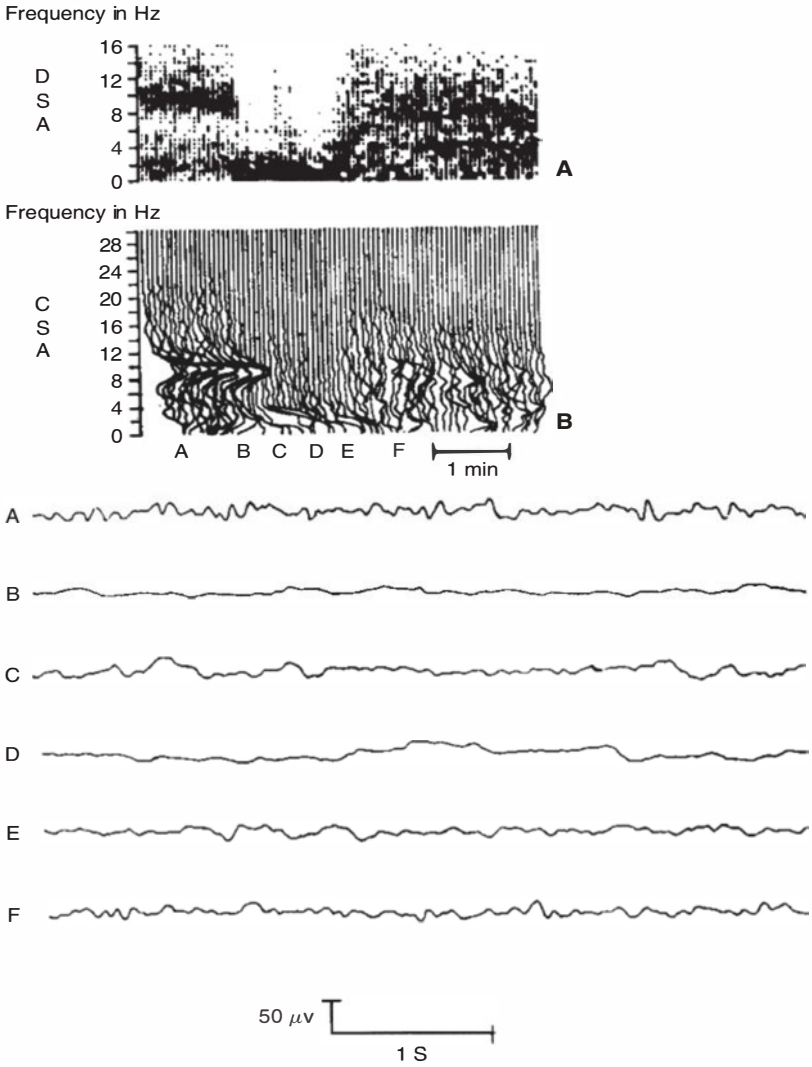

Figure 17.3 An example of density spectral analysis **(A)** and the unprocessed electroencephalogram (EEG) **(B)** compressed during a period of marked hypotension during initiation of bypass. Slowing waveform activity in the unprocessed EEG (B to E) is also evident in the density modulated spectral array (DSA) and compressed spectral array (CSA). (Reprinted with permission from Levy W, Shapiro HM, Maruchak G, et al. Automated EEG processing for intraoperative monitoring. *Anesthesiol.* 1980;53:223.)

In 1961, Lassen and Ingva described the intracarotid injection method of CBF determination. The technique involves injecting a radioactive tracer, ^{85}Kr or ^{133}Xe, as a bolus into the cerebral arterial supply and following the cerebral washout with external scintillation counting. Use of external scintillation counters makes it possible to determine regional CBF, and the sensitivity of the technique is improved by increasing the number of detectors. The tracer is injected directly into either an

internal carotid or vertebral artery, minimizing the number of counts obtained from the extracranial circulatory distribution. This method assumes that the tracer mixes completely with brain. Because the tracer is almost completely exhaled on passage through the lungs, it has essentially no recirculation. A typical tracer washout curve in normal brain is the summation of two exponential curves. Two separate flows, fast (gray matter) and slow (white matter), can be calculated using compartmental analysis.

The more noninvasive techniques to determine CBF are the inhalation and intravenous techniques. The inhalation method involves a 1-minute period of inhalation of ^{133}Xe followed by a 10-minute period of washout with external detection. The washout of tracer from the brain is similar to that obtained with intra-arterial injection except that, because of mixing in the heart and the lungs, the input of tracer is not instantaneous. Because the slow component of CBF is contaminated by extracranial clearance of the tracer, the noninvasive methods are suited primarily for determination of gray matter flow. The inhalation and intravenous methods may be less reliable in the presence of pulmonary disease because the end-tidal concentration of tracer may not adequately reflect arterial concentration. With these techniques, extracranial contamination can result in an underestimation of CBF, and under extremely low flow states, they may not give reliable quantitative information.

One thing to bear in mind with all tracer washout techniques is that, in general, they only provide flow information about cortical blood flow and not about deeper structures. Furthermore, with any of these techniques, CBF is a calculated number, and it will vary depending on the specific technique used to measure it. Average global CBF is 50 mL/100 g/min, gray matter flow is 80 mL/100 g/min, and white matter flow is 20 mL/100 g/min. A measured flow intraoperatively of greater than 24 mL/100 g/min is considered to be sufficient and that of less than 18 mL/100 g/min is inadequate. The specific flow differences compatible with ischemia depend on the anesthetic agents used. The expense and expertise required to collect and interpret CBF data have limited its use to only a few centers.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*, 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1117–1122.

Bell BA. A history of the study of the cerebral circulation and the measurement of cerebral blood flow. *Neurosurgery*. 1984;14:238–246.

C.5. Does internal carotid stump pressure accurately reflect cerebral perfusion?

The internal carotid stump pressure, the pressure in the portion of the internal carotid artery cephalad to the carotid cross-clamp, has been used to determine whether CBF during cross-clamping was adequate to avoid neuronal damage. The stump pressure presumably reflects pressure transmitted through collateral vessels. Maintaining stump pressures from 25 to 70 mm Hg has been described as necessary to avoid neurologic injury. Nevertheless, this range of stump pressures may not reliably represent the adequacy of collateral CBF, because it does not correlate consistently with changes in the EEG, regional CBF, or changes in the neurologic status of the awake patient. Furthermore, anesthetic agents can alter carotid stump pressure without changing regional CBF. Inadequate stump pressures have been demonstrated when measured regional CBF was adequate. Therefore, if shunting during carotid endarterectomy were to be done only on the basis of stump pressures, some patients would unnecessarily receive shunts.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*, 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1117–1122.

Harada RN, Comerota AJ, Good GM, et al. Stump pressure, electroencephalographic changes, and the contralateral carotid artery: another look at selective shunting. *Am J Surg.* 1995;170:148–153.

Kelly JJ, Callow AD, O'Donnell TF, et al. Failure of carotid stump pressure: its incidence as a predictor for a temporary shunt during carotid endarterectomy. *Arch Surg.* 1979;114:1361–1366.

C.6. Discuss somatosensory evoked potentials (SSEPs) as a monitor of CBF during carotid endarterectomy.

SSEPs are a specialized form of electrophysiologic monitoring that reflects the presence of intact sensory pathways from a stimulated peripheral nerve to the cortex, where electrical activity is monitored. Evidence exists that distortion of certain waveforms is associated with ischemia. These SSEP changes are not consistently associated with changes in the EEG. Questions have been raised regarding whether SSEPs can overpredict the presence of ischemia and the need for shunting. If SSEPs are a useful indicator of ischemia, they may be used when ischemia cannot be detected on an electroencephalographic tracing, such as during barbiturate anesthesia. During barbiturate anesthesia, the isoelectric EEG can only indicate that neurons are quiet. It cannot indicate whether these same neurons are ischemic. The SSEP tracing would remain intact with barbiturate anesthesia and, therefore, would potentially be more useful as a clinical monitor. Patients who have had strokes have some asymmetry in baseline SSEP waveforms. This asymmetry does not appear to affect the SSEP as an effective clinical monitor, which may also be a relative advantage over the EEG in patients with prior cerebral vascular accidents.

Lam AM, Teturswamy G. Monitoring of evoked responses during carotid endarterectomy and extracranial-intracranial anastomosis. *Int Anesthesiol Clin.* 1984;22:107.

Manninen PH, Tan TK, Sarjeant RM. Somatosensory evoked potential monitoring during carotid endarterectomy in patients with a stroke. *Anesth Analg.* 2001;93:39–44.

Moorthy SS, Markand ON, Dilley RS, et al. Somatosensory-evoked responses during carotid endarterectomy. *Anesth Analg.* 1982;61:879–883.

C.7. Describe the role of the transcranial Doppler as a monitor of cerebral perfusion during carotid endarterectomy.

By allowing for continuous assessment of the velocity of the blood flow in the ipsilateral middle cerebral artery, transcranial Doppler may be useful throughout carotid endarterectomy. It can aid in determining the need for a shunt by detecting a decrease in the middle cerebral artery blood flow velocity with placement of the carotid cross-clamp. It allows for continuous assessment of shunt function. It can be used to assess the adequacy of pharmacologically induced intraoperative hypertensive therapy. Transcranial Doppler also allows for the detection of air or particulate embolization. The disadvantage of transcranial Doppler is that it is technically demanding and not obtainable in approximately 20% of patients.

A good correlation has been shown between intraoperative electroencephalography and transcranial Doppler. Patients who have unchanged EEGs have a middle cerebral artery velocity of 24.1 cm per second during cross-clamping, whereas those with a middle cerebral artery velocity of 14.7 cm per second develop electroencephalographic changes. The ratio of the mean velocity while the cross-clamp is in place compared with the mean velocity before placement of the clamp may also be used to predict alteration in neurologic function. A ratio below 0.4 detects 97% of patients with electroencephalographic evidence of cerebral ischemia.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*, 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1117–1122

Grubhofer G, Plochl W, Skolka M, et al. Comparing Doppler ultrasonography and cerebral oximetry as indicators for shunting in carotid endarterectomy. *Anesth Analg.* 2000;91:1339–1344.

Jansen C, Vriens EM, Eikelboom BC, et al. Carotid endarterectomy with transcranial Doppler and electroencephalographic monitoring: a prospective study in 130 operations. *Stroke* 1993;24:665–669.

Jorgensen LG, Schroeder TV. Transcranial Doppler for detection of cerebral ischaemia during carotid endarterectomy. *Eur J Vasc Surg.* 1992;6:142–147.

Schneider PA, Rossman ME, Torem S, et al. Transcranial Doppler in the management of extracranial cerebrovascular disease: implications in diagnosis and monitoring. *J Vasc Surg.* 1988;7:223–231.

C.8. What type of anesthesia will you choose for this patient?

Patients undergoing carotid endarterectomy may have either regional or general anesthesia. Each type of anesthesia has advantages and disadvantages that must be considered when choosing the optimal anesthetic for each patient. Benefits of general anesthesia include a still patient and a quiet operative field, early control of the airway and ventilation, and the ability to "protect" the brain should ischemia, which cannot be eliminated, develop. A disadvantage of general anesthesia is the inability to perform repeated neurologic evaluations during surgery. Therefore, patients receiving general anesthesia should have their CBF or neurologic function monitored as previously discussed.

The primary advantage of a regional anesthetic is that the patient remains awake allowing for repeated neurologic evaluations. Although anecdotal reports support that regional anesthesia allows for greater stability of blood pressure, decreased requirement for vasoactive medications to support blood pressure, and decreased incidence of perioperative myocardial infarction, further outcome studies are warranted. Potential complications associated with regional anesthesia include the following:

- Seizures
- Alteration of mental status with cerebral ischemia
- Loss of patient cooperation associated with cerebral hypoperfusion, inadequate ventilation, and sedation

A meta-analysis of three randomized studies of 143 patients and 17 nonrandomized retrospective studies demonstrated that within 30 days of operation, there was a 50% reduction in the relative odds for death, stroke, myocardial infarction, and pulmonary complications with regional anesthesia. Nevertheless, there are still no large randomized prospective studies to draw definitive conclusions in terms of which type of anesthesia is optimal.

Allen BT, Anderson CB, Rubin BG, et al. The influence of anesthetic technique on perioperative complications after carotid endarterectomy. *J Vasc Surg.* 1994;19:834–843.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*, 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1117–1122.

Corson JD, Chang BB, Shah DM, et al. The influence of anesthetic choice on carotid endarterectomy outcome. *Arch Surg.* 1987;122:807–812.

Ombrellaro MP, Freeman MB, Stevens SL, et al. Effect of anesthetic technique on cardiac morbidity following carotid artery surgery. *Am J Surg.* 1996;171:387–390.

Stoneham MD, Knighton JD. Regional anaesthesia for carotid endarterectomy. *Br J Anaesth.* 1999;82:910–919.

C.9. How will you induce and maintain general anesthesia in this patient?

Following preoxygenation, all anesthetics should be titrated slowly with special attention to their effect on the patient's blood pressure. Control of the airway should be taken as soon as the patient is no longer able to breathe adequately to maintain normocarbia. While breathing oxygen, the patient is given small doses of fentanyl and reminded to breathe to maintain normocapnea. Opioids are administered until the patient is comfortably sedated. Lidocaine is administered intravenously at least 2 minutes before laryngoscopy and intubation to blunt the hyperdynamic response to airway manipulation. Following administration of thiopental, propofol, or etomidate, controlled ventilation is instituted with 100% oxygen to avoid hypoxia and hypercarbia. A muscle relaxant is administered to facilitate endotracheal intubation. Succinylcholine should be avoided in hemiparetic patients because of the possibility of a hyperkalemic response to its administration. Nondepolarizing muscle relaxants with significant hemodynamic effects such as sympathomimetic activity, vagolysis, or histamine release should be avoided. Once the patient is relaxed, an expeditious laryngoscopy and intubation are performed. The time spent intubating the patient's trachea is minimized to decrease the hemodynamic response to airway manipulation.

During the induction and intubation sequence, the patient's blood pressure is kept in her normal range by the use of vasopressors or vasodilators as indicated. Short-acting and easily titratable vasoactive medications should be chosen to facilitate blood pressure control.

Anesthesia can be maintained with a combination of volatile anesthetics and opioids. The addition of opioids to an isoflurane anesthetic will decrease heart rate, reduce the requirements for volatile anesthetics, and, when properly dosed, allow for a prompt, smooth emergence from general anesthesia. Their use should not be avoided because of anecdotal reports of adverse neurologic outcome after focal ischemia in rodents. Any anesthetic regimen is suitable if it provides hemodynamic stability, does not exacerbate cerebral ischemia, and allows for a prompt emergence from anesthesia at the conclusion of surgery.

Maintenance of a light anesthetic appears to have several advantages over deep anesthesia. It allows ischemic patterns on the EEG to be recognized easily. It also facilitates maintenance of the patient's blood pressure. In addition, administration of a light anesthetic, compared to a deep anesthetic using phenylephrine to maintain blood pressure, results in a lower incidence of perioperative myocardial infarction.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*, 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1117–1122.

Barone FC, Feuerstein GZ, White RF. Brain cooling during transient focal ischemia provides complete neuroprotection. *Neurosci Biobehav Rev*. 1997;21:31–44.

Schmid-Elsaesser R, Hungerguber E, Zausinger S, et al. Combination drug therapy and mild hypothermia: a promising treatment strategy for reversible, focal cerebral ischemia. *Stroke*. 1999;30:1891.

Smith JS, Roizen MF, Cahalan MK, et al. Does anesthetic technique make a difference? Augmentation of systolic blood pressure during carotid endarterectomy: effects of phenylephrine versus light anesthesia and of isoflurane versus halothane on the incidence of myocardial ischemia. *Anesthesiology*. 1988;69:846–855.

C.10. How would you proceed if the patient were to receive regional anesthesia?

Patient cooperation is essential for a regional anesthetic to proceed successfully. For a patient to be adequately anesthetized, a sensory blockade is required in the C2 to C4 dermatomes. This can be accomplished with either deep or superficial cervical plexus

blocks. In doing the blocks, care must be taken not to excessively palpate the neck, because part of the plaque in the carotid artery may dislodge and embolize.

Superficial cervical plexus blocks are performed by infiltrating along with middle third of the posterior border of the sternocleidomastoid muscle with local anesthesia. Deep cervical plexus blocks are performed with three injections along a line drawn from Chassaignac tubercle (C6) to the mastoid process. The C4 nerve root is located at the intersection of that line with one drawn horizontally from the lower border of the mandible. C2 and C3 are located by dividing the distance between the mastoid process and the horizontal line into thirds. Alternatively, a single injection of local anesthetic can be made on the line between the mastoid process and Chassaignac tubercle at the level of C4 with the needle directed medially and slightly caudad.

Patients receiving regional anesthesia must be both cooperative and not oversedated with intravenous medications. If they are unable to cooperate and become obtunded, the primary advantage of regional anesthesia (which is continuous neurologic evaluation) is lost. Intravenous sedation therefore must be given judiciously, if at all, to these patients.

Bosiljevac JE, Farha SJ. Carotid endarterectomy: results using regional anesthesia. *Am J Surg*. 1980;46:403–408.

Brown DL. *Atlas of Regional Anesthesia*. 2nd ed. Philadelphia: WB Saunders; 1999:181–183.

Cousins MJ, Bridenbaugh PO, eds. *Neural Blockade in Clinical anesthesia and Management of Pain*. 3rd ed. Philadelphia: Lippincott-Raven; 1997:507–513.

Peitzman AB, Webster MW, Loubeau J, et al. Carotid endarterectomy under regional (conductive) anesthesia. *Ann Surg*. 1982;196:59–64.

C.11. Discuss the effects of anesthetics on CBF.

It is important to remember that all general anesthetics affect CBF and cerebral metabolic oxygen consumption. This can be used to the anesthesiologist's advantage when the decrease in oxygen consumption is greater than the decrease in CBF.

In general, volatile anesthetics are considered to be vasodilators and intravenous anesthetics to be vasoconstrictors. Ketamine is an exception because it will cause increases in both CBF and cerebral metabolic rate. Volatile anesthetics, as vasodilators, produce a dose-dependent increase in CBF. The magnitude of vasodilation is dependent on the balance between the anesthetic's intrinsic vasodilatory property and vasoconstriction secondary to its decrease in cerebral metabolic rate.

It has been suggested that anesthetic agents only affect the blood flow in normally perfused areas of the brain. If this is the case, volatile anesthetics will cause a steal phenomenon, in which the blood vessels in normal brain dilate and steal blood flow away from ischemic areas of the brain that are both already maximally vasodilated and unresponsive to the vasodilating effects of the anesthetics.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1008

Matta BF, Heath KJ, Tipping K, et al. Direct cerebral vasodilatory effects of sevoflurane and isoflurane. *Anesthesiology*. 1999;91:677–680.

C.12. Discuss the protective effects of anesthetic agents on cerebral function.

Although it has not been proved that general anesthetics afford brain protection, agents that cause the greatest decrease in cerebral metabolic oxygen consumption should lessen the risk of cerebral ischemia. Whether a particular anesthetic is optimal

for these patients is an area of discussion. Obviously, avoiding or eliminating ischemia is preferable to protecting against it.

Messick examined the effects of volatile anesthetics on critical regional CBF, that is, the regional CBF at which EEG evidence of cerebral ischemia became apparent. He found that critical regional CBF in patients receiving isoflurane was less than 10 mL/100 g/min and in patients receiving halothane was 18 to 20 mL/100 g/min. This decrease in critical CBF suggests that isoflurane may offer some protective effect. Because of its potential to cause a decrease in blood pressure and reflex increase in heart rate, it probably should not be used at high concentrations as the sole anesthetic. A significant proportion of patients with carotid artery disease also have coronary artery disease and may not tolerate the hypotension and tachycardia associated with the use of high-dose isoflurane. By using this anesthetic in low concentrations in combination with other anesthetic agents, one can better maintain hemodynamic stability while perhaps providing for an increased tolerance of cerebral hypoperfusion. Other evidence, suggests that isoflurane may not offer protection during regional cerebral ischemia.

The newer agents, sevoflurane and desflurane, have been investigated for their possible role in neuroanesthesia. Compared to isoflurane, desflurane has no significant difference in its effects on decreasing cerebral glucose utilization, increasing blood flow, and maintaining coupling between local CBF and local cerebral glucose utilization. Although sevoflurane showed no significant difference in its effects on decreasing cerebral glucose utilization, and coupling between local CBF and local cerebral glucose utilization at 1 minimum alveolar concentration, it did show less of an increase in CBF. This difference between isoflurane and sevoflurane was independent of their effects on systemic blood flow and cardiac output. Hence, desflurane and sevoflurane may have similar neuroprotective effects as isoflurane and, with their lower blood gas solubility coefficients, may promote a more rapid recovery from anesthesia, allowing faster evaluation of neurologic status.

Thiopental affords cerebral protection against focal or incomplete global cerebral ischemia. It is a cerebral vasoconstrictor, as are most other intravenous anesthetics. It will also transiently decrease cerebral metabolism to 40% to 50% of baseline. The combined effect is that cerebral metabolic oxygen consumption is decreased more than oxygen delivery. The reduction in oxygen demand is the result of inhibition of functioning neurons, which can be seen as a quiet or isoelectric EEG. When dosing barbiturates for cerebral protection, the EEG should be monitored and repeated doses given to achieve and then maintain a burst suppression pattern. Once the EEG is isoelectric, indicating lack of neuronal function, further doses of thiopental do not provide additional protection. It is generally not recommended that thiopental be used for cerebral protection during carotid endarterectomy. As mentioned previously, avoidance of ischemia is preferable to its treatment. If thiopental is used, the EEG, because of its isoelectricity, becomes useless as a monitor of cerebral ischemia. This is especially problematic if selective shunting is to be done. Furthermore, the doses of thiopental required to suppress the EEG may cause hypotension and a delayed emergence from anesthesia.

Barbiturate use to minimize the possibility of cerebral ischemia has been advocated for the patient undergoing carotid bypass procedures in which temporary occlusion of the recipient vessel is required. Whether treatment of patients with a 3- to 5-mg per kg dose of thiopental affects their outcome in terms of neurologic deficit is not known, though it has been shown to be efficacious in animal models.

Dexmedetomidine is a selective α_2-adrenergic agonist with sedative, analgesic, and anxiolytic properties. It does not cause respiratory depression. In animal studies, dexmedetomidine reduces ischemic damage after transient and permanent ischemia. Its mechanism of neuroprotection is still unclear. One hypothesis suggests that with the onset of cerebral ischemia, one of the initial responses in the central nervous system is the excessive release of norepinephrine and glutamate during

energy failure. If the increase in norepinephrine release is a causative component of injury, an α_2-adrenergic agonist may decrease the damage afforded by cerebral ischemia. Dexmedetomidine has been shown to reduce arousal and decrease CBF in volunteers.

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Hicks RG, Kerr DR, Horton DA. Thiopentone cerebral protection under EEG control during carotid endarterectomy. *Anaesth Intensive Care*. 1988;14:22–28.

Holzer A, Greher M, Hetz H, et al. Influence of aortic blood flow velocity on changes of middle cerebral artery blood flow velocity during isoflurane and sevoflurane anaesthesia. *Eur J Anaesthesiol*. 2001;18:238–244.

Jolkkonen J, Puurunen K, Koistinaho J, et al. Neuroprotection by the α_2-adrenoceptor agonist, dexmedetomidine, in rat focal cerebral ischemia. *Eur J Clin Pharmacol*. 1999;372:31–36.

Kuhmonen J, Haapalinna A, Sivenius J. Effects of dexmedetomidine after transient and permanent occlusion of the middle cerebral artery in the rat. *J Neural Transm*. 2001;108:261–271.

Kuhmonen J, Pokorny J, Miettinen R, et al. Neuroprotective effects of dexmedetomidine in the gerbil hippocampus after transient global ischemia. *Anesthesiology*. 1997;87:371–377.

Lenz C, Rebel A, van Ackern K, et al. Local cerebral blood flow, local cerebral glucose utilization, and flow-metabolism coupling during sevoflurane versus isoflurane anesthesia in rats. *Anesthesiology*. 1998;89:1480–1488.

Lenz C, Frietsch T, Futterer C, et al. Local coupling of cerebral blood flow to cerebral glucose metabolism during inhalational anesthesia in rats. *Anesthesiology*. 1999;91:1720–1723.

Matta BF, Heath KJ, Tipping K, et al. Direct cerebral vasodilatory effects of sevoflurane and isoflurane. *Anesthesiology*. 1999;91:677–680.

Messick JM Jr, Casement B, Sharbrough FW, et al. Correlation of regional cerebral blood flow (rCBF) with EEG changes during isoflurane anesthesia for carotid endarterectomy: critical rCBF. *Anesthesiology*. 1987;66:344–349.

Michenfelder JD, Sundt TM, Fode N, et al. Isoflurane when compared to enflurane and halothane decreases the frequency of cerebral ischemia during carotid endarterectomy. *Anesthesiology*. 1987;67:336–340.

Moffat JA, McDougall MJ, Brunet D, et al. Thiopental bolus during carotid endarterectomy–rational drug therapy? *Can Anaesth Soc J*. 1983;30:615–622.

Nehls DG, Todd MM, Spetzler RF, et al. A comparison of the cerebral protective effects of isoflurane and barbiturates during temporary focal ischemia in primates. *Anesthesiology*. 1987;66:453–464.

Nussmeier NA, Arlund C, Slogoff S. Neuropsychiatric complications after cardiopulmonary bypass: cerebral protection by a barbiturate. *Anesthesiology*. 1986;64:165–170.

Shapiro HM. Barbiturates in brain ischaemia. *Br J Anaesth*. 1985;57:82–95.

Prielipp RC, Wall MH, Tobin JR, et al. Dexmedetomidine-induced sedation in volunteers decreases regional and global cerebral blood flow. *Anesth Analg*. 2002;95:1052–1059.

C.13. How will you manage this patient's ventilation under general anesthesia?

Because carbon dioxide is a potent cerebral vasodilator, it was initially recommended that patients undergoing carotid endarterectomy be hypoventilated intraoperatively to achieve hypercarbia and cerebral vasodilation. It is now well accepted that hypercapnea should be avoided in patients with carotid artery disease. Carbon dioxide causes vasodilation in normally reactive, nonischemic, vascular beds. In patients with carotid

artery disease, this means that blood flow is diverted away from the already maximally dilated vessels in the territory of the occluded carotid and toward normal areas of the brain. This decrease in regional CBF in ischemic areas of the brain with increased CBF in normal areas of the brain is known as *intracerebral steal*.

Other authors have recommended extreme hypocapnea during carotid endarterectomy, reasoning that this would result in an "inverse steal" or "Robin Hood" phenomenon. Hypocapnea will cause constriction of cerebral vessels in normally perfused areas of the brain, possibly diverting blood flow into the maximally vasodilated, unreactive, hypoperfused regions of the brain. Clinical trials have been unable to demonstrate any benefit from hypocapnea, and animal studies have shown that it may, in fact, exacerbate ischemia. This most likely happens not only because of intense vasoconstriction, but also because of a leftward shift of the oxyhemoglobin dissociation curve so that hemoglobin is less able to give its oxygen to tissues.

The general recommendation for patients with cerebrovascular disease is that normocarbia or mild hypocarbia be maintained. After repair of their carotid stenosis, some patients will have a marked hyperemia with CBF of 100 mL/100 g/min. In these patients, decreasing both blood pressure and arterial carbon dioxide tension to decrease their CBF is indicated. Without a decrease in CBF, these patients are at risk for postoperative intracerebral hemorrhage.

Baker WH, Rodman JA, Barnes RW, et al. An evaluation of hypocarbia and hypercarbia during carotid endarterectomy. *Stroke*. 1976;7:451–454.

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Roizen MF, ed. *Anesthesia for Vascular Surgery*. New York: Churchill Livingstone; 1990:128–129.

C.14. How will you manage this patient's blood pressure intraoperatively?

Various factors need to be considered in the blood pressure management of patients undergoing carotid endarterectomy. In the patient with carotid artery disease, a loss of autoregulation occurs in ischemic areas of the brain. In areas of chronic hypoperfusion, vessels are maximally vasodilated and unresponsive to vasomotor stimuli. Perfusion in these ischemic areas is pressure dependent.

During cerebral arterial occlusion, systemic blood pressure may need to be increased to augment collateral blood flow. The primary collateral pathways include the Willisian channels. If Willisian channels are not available, either because of the patient's anatomy or a therapeutic intervention, secondary collateral channels are available that bridge adjacent major vascular territories. These pathways are known as the *pial-to-pial collateral* or *leptomeningeal* pathways.

Because of the adjustment of the autoregulatory limits in hypertensive patients and because of a lack of autoregulation in ischemic areas of the brain, hypotension should be avoided. The patient's blood pressure should be maintained in its high normal range. During arterial occlusion, the only practical way to increase collateral blood flow may be by increasing the collateral perfusion pressure by raising the systemic blood pressure. The extent to which the blood pressure should be raised depends on the nature of the disease. During deliberate hypertension, the systemic blood pressure is raised by 30% to 40% above the baseline or until ischemic symptoms resolve. Both maintenance of and increases in blood pressure can be accomplished with light anesthesia and, when necessary, infusion of the α-agonist phenylephrine. Phenylephrine has no direct effect on the cerebral vasculature; therefore, cerebral perfusion is increased by an elevation in the cerebral perfusion pressure. Phenylephrine increases blood pressure, cerebral perfusion pressure, stump pressure, and regional CBF. It also increases myocardial oxygen consumption. Because it increases after-

load, care must be taken when it is used in patients with coronary artery disease. It may exacerbate ischemia and failure. In patients with coronary artery disease, blood pressure should not be increased above baseline unless evidence of cerebral ischemia develops. Extreme increases in blood pressure can and should be managed with easily titratable intravenous vasodilators such as sodium nitroprusside or nitroglycerin.

After the bifurcation of the carotid artery is exposed, the surgeon often infiltrates the carotid sinus with lidocaine to eliminate the unpredictable hemodynamic response to manipulation of the carotid artery.

Once the stenosis has been relieved and the carotid cross-clamp removed, the patient's blood pressure should be maintained in its low normal range. This lowering of blood pressure offers several advantages. It decreases myocardial oxygen consumption by decreasing the work of the heart, it decreases the amount of stress on the suture line in the carotid artery, and finally, it minimizes the possibility of reperfusion hemorrhage.

Aaslid R, Lindegaard KF, Sorteberg W, et al. Cerebral autoregulation dynamics in humans. *Stroke*. 1989;20:45–52.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*, 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1117–1122.

Boysen G, Engell HC, Henrickson H. The effect of induced hypertension on internal carotid artery pressure and regional cerebral blood flow during temporary carotid clamping for endarterectomy. *Neurology*. 1972;22:1133–1144.

Smith JS, Roizen MF, Cahalan MK, et al. Does anesthetic technique make a difference? Augmentation of systolic blood pressure during carotid endarterectomy: effects of phenylephrine versus light anesthesia and of isoflurane versus halothane on the incidence of myocardial ischemia. *Anesthesiology*. 1988;69:846–855.

Young WL, Pile-Spelman J. Anesthetic considerations for interventional neuroradiology (review). *Anesthesiology*. 1994;80:427–456.

C.15. Discuss reperfusion injury following carotid endarterectomy and carotid artery stenting.

Reperfusion injury involves cerebral hemorrhage or the development of cerebral edema after obstruction to flow through the carotid artery has been relieved. Although rare, it is an often fatal complication of carotid endarterectomy. Patients with a previous stroke are most likely to suffer reperfusion hemorrhage, but it can occur in otherwise normal brain tissue. Poorly controlled blood pressure after the carotid cross-clamp has been removed contributes to this complication. One proposed mechanism for this injury is that once flow is returned to normal, vascular beds in previously hypoperfused areas of the brain are unable to respond properly with vasoconstriction. They are unable to maintain normal flow with increased perfusion. Because hypoperfusion distal to the carotid stenosis has been long-standing, these vessels have lost their ability to autoregulate. Once the carotid stenosis is eliminated, the perfusion pressure distal to the former site of the stenosis is markedly increased. Because of the lack of autoregulation in this area, CBF increases with increasing perfusion. The patients at highest risk for reperfusion injury have the greatest degree of stenosis and the greatest pressure drop across the carotid lesion. Again, maintaining blood pressure control with antihypertensive medications once the carotid obstruction is eliminated decreases the incidence of reperfusion injury.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*, 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1117–1122.

Breen JC, Caplan LF, DeWitt LD, et al. Brain edema after carotid surgery. *Neurology*. 1996;46:175–181.

Peipgras D, Morgan M, Sundt T, et al. Intracerebral hemorrhage after carotid endarterectomy. *J Neurosurg.* 1988;68:532–536.

Schroeder T, Sillisen H, Sorensen O, et al. Cerebral hyperperfusion following carotid endarterectomy. *J Neurosurg.* 1987;66:824.

Solomon R, Loftus C, Quest DQ, et al. Incidence and etiology of intracerebral hemorrhage following carotid endarterectomy. *J Neurosurg.* 1986;64:29.

C.16. What intravenous fluids will you give this patient intraoperatively?

Because moderate hyperglycemia has been shown to worsen neurologic outcome after ischemia, care must be taken to avoid increasing the patient's glucose with exogenously administered dextrose. Intravenous fluids such as Normosol R, lactated Ringer's solution, or normal saline would be appropriate choices for patients undergoing carotid endarterectomy.

These patients should not be vigorously hydrated intraoperatively. It is best to limit their intraoperative fluids to what is required for maintenance, with additional colloid and blood replacement being given as needed. Intraoperative overhydration may lead to some of the frequently observed postoperative hypertension and in patients with myocardial disease may exacerbate congestive heart failure.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia.* 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1117–1122.

Li PA, Siesjo BK. Role of hyperglycaemia-related acidosis in ischaemic brain damage. *Acta Physiol Scand.* 1997;161:567–580.

Pulsinelli WA, Levy DE, Sigsbee B, et al. Increased damage after ischemic stroke in patients with hyperglycemia with or without established diabetes mellitus. *Am J Med.* 1983;74:540–544.

Pulsinelli WA, Waldman S, Rawlingson D, et al. Moderate hyperglycemia augments ischemic brain damage: a neuropathologic study in the rat. *Neurology.* 1983;33:222–233.

D. Postoperative Management

D.1. The patient does not "wake up" from general anesthesia. Why?

Once other causes of slow emergence from general anesthesia (such as hyperglycemia or hypoglycemia, hypothermia, anesthetic overdose, hypercarbia, and hypoxemia) have been ruled out, the possibility of an adverse intraoperative event having occurred needs to be considered. Patency of the carotid artery should be evaluated. This can be done by Doppler studies while the patient is still in the operating room. If no blood flow is seen in the carotid artery, the incision can be reexplored immediately. If Doppler studies are normal, the possibility of a cerebral infarction from prolonged hypoperfusion or from emboli must be considered. The patient should remain intubated while further studies, including a CT scan and cerebral angiography, are done as expeditiously as possible. The incidence of new perioperative neurologic deficits is 3% in centers where the operation is done commonly.

Graber JN, Vollman RW, Johnson WC, et al. Stroke after carotid endarterectomy: risk as predicted by preoperative computerized tomography. *Am J Surg.* 1984;147:492–497.

Paciaroni M, Eliasziw M, Kappelle LJ, et al. Medical complications associated with carotid endarterectomy. *Stroke.* 1999;30:1759–1763.

D.2. Postoperatively, the patient's blood pressure is 170/96 mm Hg. Will you treat this?

This patient's blood pressure needs to be carefully controlled because postoperative hypertension is associated with bleeding at the operative site, myocardial ischemia, arrhythmias, intracerebral hemorrhage, and cerebral edema.

Hypertension is observed more commonly than hypotension after carotid endarterectomy. Causes of hypertension include hypoxemia, hypercarbia, pain, and a full bladder. Obviously, if any or all of these causes are present, they need to be dealt with promptly and appropriately. Another common cause of postoperative hypertension and tachycardia is blunting of the carotid baroreceptor mechanism secondary to carotid sinus dysfunction caused by surgical trauma. If this is the cause of hypertension, therapy with antihypertensive agents should be started.

This patient's blood pressure should be maintained in her low normal range postoperatively. Elevated blood pressure can be treated with hydralazine in 5-mg increments or, if the patient is not bradycardic, labetalol may be used in 10-mg increments. Alternatively, infusions of sodium nitroprusside or nitroglycerin may be used. β-Blockade with metoprolol or an infusion of esmolol may be added to this regimen.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1117–1122.

Wong JH, Findlay JM, Suarez-Almazor ME. Hemodynamic instability after carotid endarterectomy: risk factors and associations with operative complications. *Neurosurgery*. 1997;41:35–41.

D.3. What immediate postoperative complications might you expect?

Immediate postoperative complications include neurologic deficits, hemodynamic instability, and respiratory insufficiency. Evaluation of the North American Symptomatic Carotid Endarterectomy Trial showed that 8.1% of patients had medical complications: 1% with myocardial infarctions, 7.1% with other cardiovascular disorders such as arrhythmias and congestive heart failure, 0.8% with respiratory complications, 0.4% with transient confusion, and 0.7% with other complications. Carotid endarterectomy is 1.5 times more likely to be associated with complications in patients with a history of cardiac disease or hypertension.

Postoperative neurologic complications are usually embolic in nature, occurring during surgery. Other neurologic complications result from reperfusion injury and intracranial hemorrhage.

Circulatory instability is common after carotid endarterectomy, with either hypotension or hypertension being observed. Hypotension may have any of several causes, as does hypertension, as noted previously. These include hypovolemia, depression of the circulation by residual anesthetics, prolonged effect of intraoperatively administered antihypertensives, dysrhythmias, and myocardial ischemia. Each of these causes needs to be sought and, if present, treated appropriately. Another possible cause of hypotension is an excessive reflex response because of increased sensitivity of the carotid sinus after exposure of the baroreceptor mechanism to a higher pressure with removal of the plaque. If this is the cause, therapy needs to be instituted with fluids and vasopressors.

Postoperative respiratory insufficiency is a rare but potentially life-threatening complication. This can be due to vocal cord paralysis from intraoperative traction on the laryngeal nerves. Should this present with inability to protect the airway, the patient should be reintubated immediately.

A prospective trial found that 12.5% of patients had nerve injuries after carotid endarterectomy, but all were transient, lasting from 1 week to 37 months. No patient

had life-threatening respiratory insufficiency from the nerve injuries. The most commonly injured nerves were the hypoglossal, recurrent laryngeal, superior laryngeal, and greater auricular nerves.

Airway obstruction can also occur from hematoma formation at the operative site, from either arterial or venous bleeding. The hematoma needs to be evacuated as quickly as possible and, depending on ventilatory status, the patient may need to be intubated. This is most easily done after evacuation of the hematoma if the clinical condition allows.

Supraglottic edema may also be a rare cause of postoperative upper airway obstruction after carotid endarterectomy. CT analysis of airways postoperatively showed reduction in the volume of the airway in all patients, with a greater reduction seen in intubated patients (63% ± 9%) than in nonintubated patients (32% ± 7%).

Tension pneumothorax can result from air dissecting through the wound and the mediastinum to the pleura. This diagnosis should be considered in all patients after carotid endarterectomy who seem to have respiratory distress and no evidence of upper airway obstruction. Absence of breath sounds over half of the chest and hemodynamic instability would support this diagnosis.

Chemoreceptor function is irreversibly suspended in most patients after carotid endarterectomy for up to 10 months. Lack of chemoreceptor function means that there is a loss of circulatory response to hypoxia and an increase in resting $Paco_2$ of approximately 6 mm Hg. This complication is potentially very serious, and one needs to be most concerned about its development in patients who have had a previous contralateral carotid endarterectomy, where function may be lost bilaterally. In all patients after carotid endarterectomy, supplemental oxygen should be provided and opioids administered cautiously.

Ballotta E, Da Giau G, Renon L, et al. Cranial and cervical nerve injuries after carotid endarterectomy: a prospective study. *Surgery*. 1999;125:85–91.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1117–1122.

Carmichael FJ, McGuire GP, Wong DT, et al. Computed tomographic analysis of airway dimensions after carotid endarterectomy. *Anesth Analg*. 1996;83:12–17.

Paciaroni M, Eliasziw M, Kappelle LJ, et al. Medical complications associated with carotid endarterectomy. *Stroke*. 1999;30:1759–1763.

Wade JC, Larson CP Jr, Hickey RF, et al. Effects of carotid endarterectomy on carotid chemoreceptor and baroreceptor function in man. *N Engl J Med*. 1970;282:823–829.

D.4. Discuss postoperative neurocognitive dysfunction following uncomplicated carotid endarterectomy.

Carotid endarterectomy will reduce the incidence of stroke in patients with high-grade carotid artery stenosis. Increasing evidence suggests that as many as 28% of surgical patients have significant neuropsychological dysfunction 1 day after carotid artery surgery. Between 9% and 23% of these patients continue to exhibit cognitive decline 1 month after surgery.

The APOE-ε4 allele has been associated with worse outcome following stroke. In a prospective trial, 75 patients undergoing carotid endarterectomy were studied. Of 75 patients, 12 (16%) possessed the APOE-ε4 allele. Of the 75 patients, 8 (11%) experienced cognitive dysfunction on postoperative day 30. One month after carotid endarterectomy, APOE-ε4-positive patients were more likely to have suffered a neurocognitive injury (42%) than APOE-ε4-negative patients (5%).

The presence of the APOE-ε4 allele increase the risk of neurocognitive dysfunction 62-fold 1 month after surgery. Diabetes and obesity also predisposed to injury.

Evidence also indicates cognitive dysfunction in patients with carotid stenosis treated with carotid artery stenting performed under cerebral embolic protection. In a prospective case control study, 41% of patients undergoing carotid stenting developed moderate to severe cognitive dysfunction compared to a matched control group. The average deficit score was significantly higher in the carotid artery stenting group at 1 day. These differences were independent of age and history of stroke or TIA. The absence of oral statin medication may increase the probability of cognitive dysfunction.

The influence of regional versus general anesthesia in postoperative subclinical cognitive dysfunction remains unclear. Most concur that multiple factors, including surgical technique, anesthetic technique, and patient status, influence postoperative outcome.

Gaudet JG, Meyers PM, McKinsey JF, et al. Incidence of moderate to severe cognitive dysfunction in patients having carotid artery stenting. *Neurosurgery*. 2009;65:325–329.

Gulur P, Nishimori M, Ballantyne JC. Regional anesthesia versus general anesthesia, morbidity and mortality. *Best Pract Res Clin Anesthesiol*. 2006;20:249–263.

Heyer EJ, Wilson DA, Sahlein DH, et al. APOE-ε4 predisposes to cognitive dysfunction following uncomplicated carotid endarterectomy. *Neurology*. 2005;65:1759–1763.

Mazul-Sunko B, Hromatko I, Tadinac M, et al. Subclinical neurocognitive dysfunction after carotid endarterectomy: the impact of shunting. *J Neurosurg Anesthesiol*. 2010;22:195–201.

CHAPTER 18

Awake Craniotomy for Mapping and Surgery in the Eloquent Cortex

Thomas A. Moore II

A 47-YEAR-OLD RIGHT-HANDED PHYSICIAN presented after two episodes of acute onset of left-sided headache associated with a change in reading comprehension and difficulty with word finding. Each episode lasted several minutes without loss of consciousness or generalized seizure activity. Magnetic resonance imaging (MRI) revealed a 4 × 5 centimeter (cm) variably marginated mass in the inferior aspect of the left temporal lobe involving the middle and inferior temporal gyri, as well as the occipitotemporal gyrus (Fig. 18.1). He was started on corticosteroids, and his symptoms did not reappear. Diffusion tensor imaging was used to determine that his optic radiations and Meyer loop were not within the lesion. Magnetoencephalography (MEG) was used to determine the location of his primary motor area. He underwent an uncomplicated awake left craniotomy with motor and language area mapping. He was discharged to home the next day. Final pathology revealed an anaplastic astrocytoma World Health Organization grade III.

A. Medical Disease and Differential Diagnosis

1. What is the eloquent cortex?
2. What is the underlying pathology?
3. What determines intracranial pressure (ICP)?
4. How does a space-occupying mass alter ICP?
5. What is autoregulation, and why is it important?
6. How is cerebral blood flow (CBF) regulated?
7. What drug therapies may be associated with this pathology?

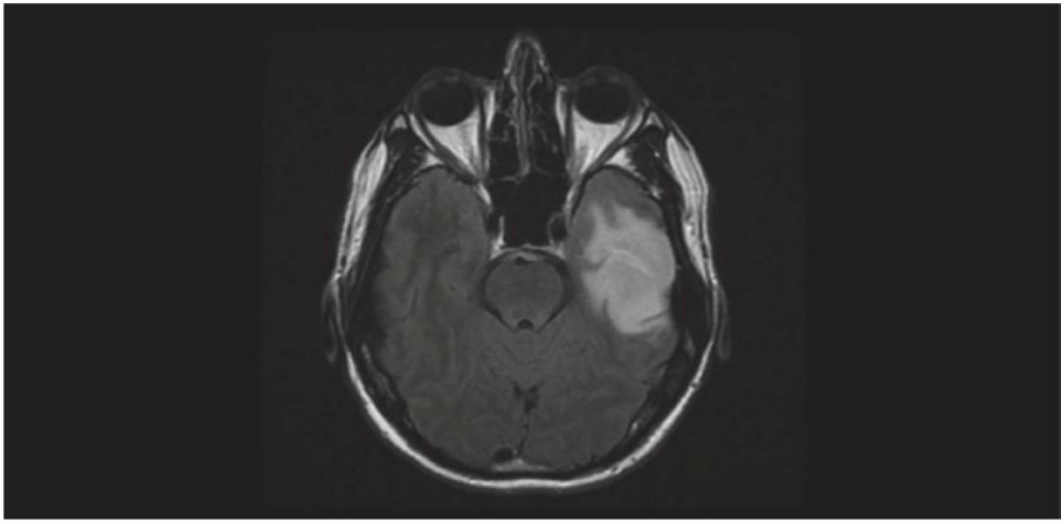

Figure 18.1 A 47-year-old man with two episodes of left-sided headaches associated with problems with reading comprehension and difficulty with word finding. He underwent an uneventful left awake craniotomy with motor and language area mapping. Final pathology was a World Health Organization grade III anaplastic oligoastrocytoma.

B. Preoperative Evaluation and Preparation

1. Why an awake craniotomy?
2. What are the current symptoms and why are they important?
3. Are there anesthetic implications from current treatment drugs?
4. What laboratory data are required?
5. What radiology data should be reviewed?
6. How do you prepare the patient for an awake craniotomy?
7. Should this patient receive premedications?
8. What precautions should be made for airway management?

C. Intraoperative Management

1. How should this patient be monitored?
2. Does this patient require invasive monitoring?
3. Can current drug therapy alter eloquent cortex mapping?
4. Why use hypertonic fluids during a craniotomy?
5. What intravenous fluids (IVFs) are recommended?
6. Would a lumbar drain for CSF removal benefit this patient?
7. Venous air embolism (VAE): Is it a concern in this case?
8. How is the eloquent cortex mapped?
9. How is an intraoperative seizure treated?
10. How will you conduct this anesthetic?

D. Postoperative management

1. What are the major concerns following craniotomy?

A. Medical Disease and Differential Diagnosis

A.1. What is the eloquent cortex?

Eloquent cortex is a term usually used to describe functional areas of the cerebral cortex associated with motor, language, and sensory activity. Traditionally, tumors or epileptic foci within or near these areas have been termed *inoperable* because of the devastation caused to the patient by injury to these neurons.

DeBenedictis A, Moritz-Gasser S, Duffau H. Awake mapping optimizes the extent of resection for low grade gliomas in eloquent areas. *Neurosurgery*. 2010;66(6):1074–1084.

A.2. What is the underlying pathology?

The underlying pathology requiring an awake craniotomy for mapping and resection within the eloquent cortex can be either a space-occupying lesion or epileptic foci. In either case, mapping of the cortical and subcortical structures with an awake and cooperative patient is necessary to minimize neurologic injury and maximize lesion resection. Mapping of the motor cortex is often done under general anesthesia, after reversal of any residual muscle relaxant, because the stimulated area(s) can usually be seen by an observer. Nevertheless, there are several potential problems. In the case of a space-occupying lesion, the neuronal pathways can become distorted secondary to the expanding mass and mislead the surgeon who is searching not only for the functional area, but also a "quiet" area of cortex through which to do the resection. In addition, these patients are frequently in a lateral decubitus position, with the side to be observed in the down position. Visualization of the patient can be further obstructed with sheets, blankets, forced warm-air blankets, and other patient-positioning devices. Hence, we tend to map the motor cortex in an awake craniotomy whenever possible.

Supratentorial brain tumors are about 31% gliomas (Fig. 18.1), 15% meningiomas, 12% metastatic lesions, and 8% pituitary tumors. Metastatic lesions are most frequently lung, breast, and gastrointestinal tract tumors. Additional space-occupying lesions include blood and blood vessels, infections, hydrocephalus, cerebral infarctions, radiation necrosis, arachnoid cysts, and cerebral edema.

These space-occupying lesions can present in various manners. The most common presentation of brain tumors is a progressive neurologic deficit (68%), usually motor weakness (45%), headache (54%), and seizures (26%). Others may present from progressive focal deficits resulting from destruction of brain tissue or compression of normal brain structures by the mass itself or peritumoral edema. Additional presentations include nausea or vomiting, vertigo, lethargy, apathy, and changes in mental status as several examples.

In addition to these various presenting signs and symptoms, asymmetric supratentorial tumors can enlarge to the point of causing a midline shift of the intracranial contents, possibly leading to herniation. The brain can be displaced across the midline beneath the falx or compressed through the tentorial incisura into the posterior fossa. As these various areas of the brain are compressed against these dense fibrous structures, stretching and shearing of the penetrating arteries can result in devastating neurologic injuries.

An area of cerebral edema surrounds most intracranial masses secondary to the disruption of the blood–brain barrier (BBB) usually associated with a localized acidosis. Vasogenic edema reflects a shift of fluid from the intravascular to the extravascular space. Cytotoxic edema represents a shift of fluid from the extracellular to the intracellular space. Vasogenic edema responds very well to corticosteroid treatment. Dexamethasone is frequently prescribed for this problem. This area of cerebral edema is known as the penumbral area and represents areas of autoregulatory dysfunction as well as BBB breakdown. The vasculature in this area of the brain is usually maximally

Table 18.1 Commonly Used Drugs in Seizure Control

TYPE OF SEIZURE	FIRST-LINE DRUG	SECOND-LINE DRUG
Generalized tonic-clonic	Carbamazepine	Clobazam
	Phenytoin	Clonazepam
	Valproate	Lamotrigine
		Phenobarbital
		Vigabatrin
		Felbamate
		Acetazolamide
Generalized absence	Valproate	Clonazepam
	Ethosuximide	Lamotrigine
		Acetazolamide
Tonic, atonic, atypical absences	Valproate	Carbamazepine
	Clobazam	Phenobarbital
	Clonazepam	Felbamate
	Lamotrigine	Acetazolamide
	Phenytoin	
Myoclonic seizures	Valproate	Phenobarbital
	Clonazepam	Acetazolamide
Simple partial, complex partial, secondarily generalized	Carbamazepine	Clobazam
	Valproate	Lamotrigine
	Phenytoin	Gabapentin
		Vigabatrin
		Phenobarbital
		Felbamate
		Acetazolamide

From Frost EAM, LaFleur JL. Awake craniotomy for deep brain stimulation. In: *Yao and Artusio's Anesthesiology: Problem-Oriented Patient Management*. 6th ed. Philadelphia: Lippincott, Williams and Wilkins; 2008:585. Used with permission.

vasodilated. Hypercapnia in surrounding normal brain causes vasodilation in the normal vasculature and may result in decreased flow to the ischemic area. Hypocapnia, on the other hand, causes vasoconstriction of the normal adjacent vascular beds, with the resultant redistribution of blood to the ischemic area. This has been referred to as the "Robin Hood" phenomenon. The formation of peritumoral edema increases the overall size of the tumor, which can lead to the same signs and symptoms as noted earlier.

Patients presenting for an awake craniotomy for excision of an epileptic foci have usually had a seizure disorder for many years and have been on numerous antiepileptic drugs (AEDs) in an attempt to control their disorder. Unfortunately, many of these patients develop adverse reactions or cannot tolerate the side effects of the AEDs and become, for practical purposes, medication failures. Table 18.1 lists the more common AEDs and the types of seizure disorder they treat.

Only patients with seizures in whom the foci are localized in an area of eloquent cortex require an awake craniotomy. Temporal lobe, hippocampal-localized foci are usually resected under general endotracheal anesthesia with intraoperative

electrocorticography. Most of these patients have had preceding intracranial strips, grids, or electrodes placed to help localize the seizure foci.

Fishman RA. Brain edema. *N Engl J Med.* 1975;293:706–711.

O'Rourke DK, Oldfield EH. Supratentorial masses: surgical considerations. In: Cottrell JE, Smith DS, eds. *Anesthesia and Neurosurgery*. 4th ed. Philadelphia: Mosby; 2001:275–295.

A.3. What determines intracranial pressure (ICP)?

The adult skull is a rigid, bony box with a fixed volume. Neonatal and infant skulls have several noncalcified portions, called fontanels, that allow the skull to deform during passage through the birth canal. These noncalcified areas also allow the volume of the skull to increase in the presence of increased ICP such as congenital hydrocephalus. Once these areas have calcified, the pediatric skull is also a rigid, fixed volume box.

The intracranial constituents are intravascular blood, cerebrospinal fluid (CSF), and the brain. As liquids, the blood and CSF are noncompressible. Although water can be extracted from the brain by use of osmotic diuretics and other hypertonic fluids, this does not result in much change in brain volume and its gel-like consistency also makes it virtually noncompressible.

ICP is a relationship of the homeostatic balance of the noncompressible contents within a fixed-volume container, the skull. The normal value is 10 to 15 mm Hg. In the early 19th century, the Monro-Kellie hypothesis was the first attempt to describe this relationship. Although several modifications of this doctrine have been made over the years as more has been learned, the basic principle still holds true: Because the intact skull is unyielding, an increase in volume of any one of the normal contents or the addition of a space-occupying lesion must be accompanied by a reduction in one or more of the normal constituents to maintain normal ICP.

Artru AA. Cerebrospinal fluid. In: Cottrell JE, Young WL, eds. *Cottrell and Young's Neuroanesthesia.* 5th ed. Philadelphia: Mosby; 2010:60–72..

Morki B. The Monro-Kellie hypothesis: adaption in CSF volume depletion. *Neurology.* 2001;56:1746–1748.

A.4. How does a space-occupying mass alter ICP?

There are limits to the balanced relationship described by the Monro-Kellie hypothesis. Figure 18.2 represents an idealized ICP–volume curve and diagrams these limitations.

The flat portion of the curve represents increasing volume with no increase in ICP. Several compensatory mechanisms are at work to keep the ICP steady. The most effective of these mechanisms is the dynamic nature of CSF. The rate of absorption increases or the rate of production decreases in light of an increase in ICP. Cerebral blood volume (CBV) is decreased by a redistribution primarily of the intracranial venous blood volume. These mechanisms work to keep the ICP at its normal value of 10 to 15 mm Hg. As the volume continues to increase, these compensatory mechanisms become exhausted and ICP starts to rise as represented by the "knee" of the graph. It is important to note that at this area of the curve, small increases in volume give rise to a much larger increase in ICP. The sharp rise in the graph demonstrates rapidly increasing ICP with even smaller increases in volume. It is vitally important to understand that as the volume continues to rise and ICP continues to increase, the risk of cerebral herniation also increases. Cerebral perfusion pressure (CPP) is also adversely affected with a rise in ICP. CPP is defined as: CPP = MAP – ICP (CVP), where MAP = mean arterial pressure and CVP = central venous pressure. This equation readily shows that an increase in ICP will lead to a decrease in CPP.

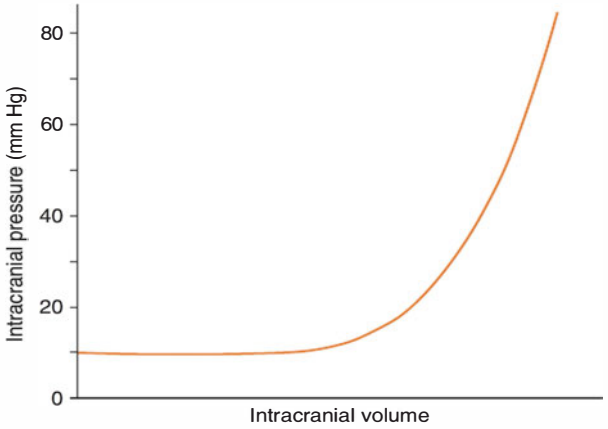

Figure 18.2 Idealized intracranial pressure–volume curve. (From Kass IS. Physiology and metabolism of the brain and spinal cord. In: Newfield P, Cottrell JE, eds. *Handbook of Neuroanesthesia*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 1999:18. Used with permission.)

Figure 18.3 shows that CBF remains at 100% for CPPs ranging from 50 to 150 mm Hg. Some have recently advocated that the lower threshold for autoregulation should be shifted more toward 70 mm Hg and the upper threshold shifted more toward 180 mm Hg. In the supine position, ICP in the normal state is effectively zero, making CPP directly related to MAP.

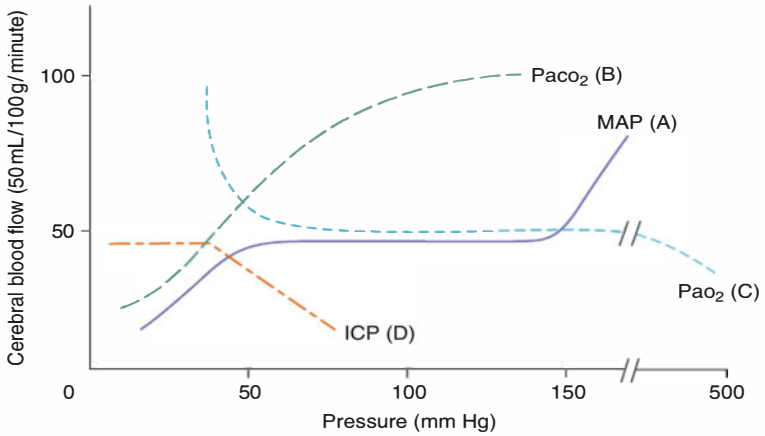

Figure 18.3 Pressure–cerebral blood flow relationships. **A.** Cerebral blood flow (CBF) autoregulation. CBF is maintained at 50 mL/100 g/min for mean arterial pressure (MAP)/cerebral perfusion pressure (CPP) = 50 to 150 mm HG. **B.** Linear relationship between $Paco_2$ and CBF for $Paco_2$ = 20 to 80 mm Hg. **C.** Pao_2 and CBF. **D.** Intracranial pressure (ICP) and CBF. (From Ravussin PA, Wilder-Smith OHG. Anesthesia for supratentorial tumors. In: Newfield P, Cottrell JE, eds. *Handbook of Neuroanesthesia*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 1999:146. Used with permission.)

A.5. What is autoregulation, and why is it important?

In its simplest form, autoregulation is a myogenic response of the vascular smooth muscle of the intracranial cerebral arterioles to maintain a nearly constant CBF in the face of changing CPP. Not all of the mechanisms controlling this action are fully understood.

When CPP becomes less than 50 mm Hg or greater than 150 mm Hg, the CBF becomes pressure passive. This response is important to keep in mind when considering the use of deliberate hypotension. A MAP of less than 50 mm Hg could theoretically cause a decrease in CPP and thereby decrease CBF to the point of causing cerebral ischemia. On the other side of the spectrum, MAPs greater than 150 mm Hg can cause disruption of the BBB and cause vasogenic edema throughout the brain, not only in the area of vasogenic edema surrounding the tumor.

The autoregulation curve is shifted to the right in the presence of chronic uncontrolled hypertension, as shown in Figure 18.4.

This is important because now the lower threshold for cerebral ischemia is higher than in the normal state. Although there is not a direct correlation between degree of hypertension and rightward shift of the autoregulatory curve, it is possible that where signs of cerebral ischemia might not have become obvious until the CPP was 30 to 40 mm Hg in the normotensive person, these signs may now occur with the CPP at 80 to 90 mm Hg, a usually normal CPP. Therefore, great care must be taken to keep the MAP near the patient's usual levels in the uncontrolled or poorly controlled hypertensive patient. On the other end of the curve, it is possible that the rightward shift adds some form of cerebral protection against perfusion breakthrough at the higher CPPs. Treatment with antihypertensive drugs modifies this rightward shift back toward the normal range. The degree to which this occurs depends both on the length of time the hypertension has been treated and the resultant decrease in blood pressure.

The type of drug used to treat hypertension may also determine the effect on autoregulation. Systemic direct-acting vasodilators without action on cerebrovascular smooth muscle and α-adrenergic and ganglionic blocking drugs should have no effect on cerebrovascular autoregulation. Systemic direct-acting vasodilators that do have

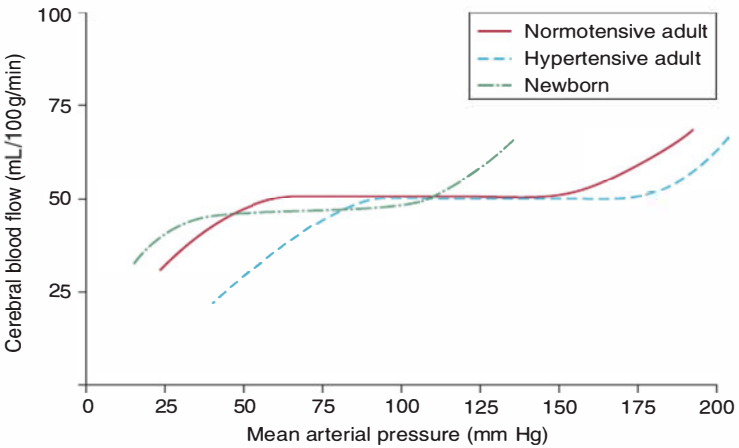

Figure 18.4 Autoregulatory curve of the cerebral vasculature in the normotensive adult, the hypertensive adult, and the newborn. (From Ravussin PA, Wilder-Smith, OHG. Anesthesia for supratentorial tumors. In: Newfield P, Cottrell JE, eds. *Handbook of Neuroanesthesia*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 1999:14. Used with permission.)

an action on the cerebrovascular smooth muscle, such as hydralazine, sodium nitroprusside, nitroglycerin, and calcium channel blockers may influence autoregulation. Treating congestive heart failure may also improve CPP by lowering CVP and thereby decreasing cerebral venous outflow pressure.

Drummond JC, Patel PM. Neurosurgical anesthesia. In: Miller, RD ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:2045–2087.

Paulson OB, Strandgaard S, Edvinson, L. Cerebral autoregulation. *Cerebrovasc Brain Metab Rev*. 1990;2:161–192.

Paulson OB, Drummond JC. The lower limit of autoregulation: time to revise our thinking? *Anesthesiology*. 1997;86:1431–1433.

A.6. How is cerebral blood flow (CBF) regulated?

CBF also responds to chemical modulation. Figure 18.3 demonstrates these relationships in the $Paco_2$ (arterial carbon dioxide partial pressure) and Pao_2 (arterial oxygen partial pressure) curves. Carbon dioxide (CO_2) concentration is the most potent modulator of CBF. Insonating the middle cerebral artery of a volunteer by means of transcranial Doppler device and asking the subject to hyperventilate will show an increase in cerebral blood velocity reflecting a decrease in CBF secondary to cerebral vascular constriction, usually within 3 to 4 breaths, a very rapid response. This principle is utilized to treat increased ICP by decreasing CBV secondary to the hyperventilation. However, this mechanism is self-limited after approximately 6 to 10 hours and will no longer provide the decreased ICP.

As shown in Figure 18.3, there is a near linear response in CBF at a $Paco_2$ between 20 and 80 mm Hg, with CBF increasing about 2% to 4% for each millimeter of mercury change in $Paco_2$. In general, doubling $Paco_2$ from 40 to 80 mm Hg doubles CBF and likewise halving $Paco_2$ from 40 to 20 mm Hg halves CBF. This represents maximal vasodilation at extreme hypercapnia and maximal vasoconstriction at extreme hypocapnia, respectively.

CBF also responds to the oxygen partial pressure. As shown in Figure 18.3, when the Pao_2 reaches approximately 50 mm Hg, a steep increase in CBF occurs as the Pao_2 continues to fall. At normal Pao_2 levels, CBF is not affected. Hyperoxia can actually cause a 10% to 15% decrease in CBF at 1 atm. Temperature can also have an effect on CBF. For each 1° C decrease in body temperature, the cerebral metabolic rate for oxygen consumption ($CMRO_2$) decreases by approximately 7%. The regulation of CBF is known to be closely coupled to the cerebral metabolism and is reflected by a parallel decrease. These changes are not homogenous with more changes seen in the cerebral and cerebellar cortices; less so in the thalamus and no difference in the hypothalamus and brainstem. During hypothermic cardiopulmonary bypass, lowering the body temperature to 26° C resulted in a 56% calculated reduction in $CMRO_2$ and a 55% reduction in CBF.

The potent inhalational agents can also increase CBF in the presence of decreasing $CMRO_2$, thus uncoupling their relationship. Increasing levels of minimum alveolar concentration can also blunt the CO_2 response or render CBF pressure passive. CO_2 reactivity is preserved during intraoperative use of opioids such as fentanyl and remifentanil.

Govier AV, Reves JG, McKay RD, et al. Factors and their influence on regional cerebral blood flow during non-pulsatile cardiopulmonary bypass. *Ann Thorac Surg*. 1984;38:592–600.

Joshi S, Ornstein O, Young WL. Cerebral and spinal cord blood flow. In: Cotrell JE, Young WL, eds. *Cottrell and Young's Neuroanesthesia*. 5th ed. Philadelphia: Mosby; 2010:17–59.

A.7. What drug therapies may be associated with this pathology?

Patients can present with intracranial pathology at any age. Patients with comorbidities may be taking medications for hypertension, diabetes mellitus, congestive heart failure or prior myocardial infarction (MI), as examples. It is not uncommon today for many patients to be on some form of antiplatelet drug whether they have suffered a MI or not. The effects of some of these drugs can be reversed with fresh frozen plasma, whereas others are not immediately reversible and need 7 to 10 days before their effect is gone.

Patients with epilepsy may be on several medications in an attempt to control their seizures. These drugs are listed in Table 18.1. Presenting signs and symptoms have been described earlier. AEDs are indicated in 26% of patient's presenting with seizures who are later diagnosed with a brain tumor.

Another 20% to 45% of patients with brain tumors will eventually develop a seizure after diagnosis. The current standard (2006) is that prophylactic AEDs should not be started in this group of patients. As a guideline, in patients with brain tumors undergoing craniotomy, prophylactic AEDs may be used, and if there is no seizure activity, they may be tapered, starting 1 week postoperatively.

As previously discussed, most intracranial mass lesions are surrounded by an area of vasogenic edema to varying extents. The use of steroids, in particular dexamethasone, are commonly used to help alleviate the problems associated with this. Dexamethasone is more beneficial, and the effect often much more dramatic in metastatic tumors than primary tumors in reducing the area of edema. The usual dosage in the corticosteroid-naïve patient is a loading dose of 10 mg IV, then 6 mg by mouth or IV every 6 hours. Doses of up to 10 mg every 4 hours have been given for severe vasogenic edema. For the patient previously diagnosed and on corticosteroids, doubling the current dose is doubled for acute deterioration.

Greenburg MS. Tumor. In: Greenburg MS, ed. *Handbook of Neurosurgery*. 7th ed. New York: Thieme; 2010: 582–769.

B. Preoperative Evaluation and Preparation

B.1. Why an awake craniotomy?

An awake craniotomy is performed when the pathologic lesion, be it a tumor or an epileptic focus, is in or near an area of eloquent cortex, as defined earlier, in an effort to preserve neurologic function.

The extent of the craniotomy is variable. Some neurosurgeons advocate a carefully planned, limited-exposure craniotomy defined with neuronavigational devices to encompass primarily the area of the lesion and immediate surrounding brain. Others advocate a large craniotomy exposing a wide cortical area for mapping. In either case, the primary goal of the surgical procedure is to obtain the greatest degree of tumor resection with as little damage to the eloquent cortex as possible and hence the least postoperative neurologic deficit.

Even with the cortex exposed, there are many challenges in identifying these areas of eloquent cortex that demand an awake and cooperative patient. As a tumor within or near the eloquent cortex grows and expands, the various neuronal pathways can become distorted from their normal anatomic locations. Ultrasonography may assist the neurosurgeon in identifying the lesion borders so testing can proceed in the surrounding areas of the cortex. Areas that do not elicit a response, respective of the area being tested, are also identified as areas of negative mapping and may serve as an entrance site for both cortical and subcortical resection as needed. Several studies have indicated that surgery through these areas of absolute negative mapping have a significantly lower incidence of both intraoperative and postoperative

neurologic deficits. There is also increasing realization that there are more cortical areas that relate to an acceptable quality of life other than the areas of eloquent cortex. Nonlanguage areas that have to do with visual and or vestibular functions, spatial awareness, cognitive function, understanding and judgment, memory, calculation, and emotion can be mapped both cortically and subcortically to help prevent postoperative complications that are usually not discussed or described.

DeBenedictis A, Moritz-Gasser S, Duffau H. Awake mapping optimizes the extent of resection for low-grade gliomas in eloquent areas. *Neurosurgery*. 2010;66(6):1074–1084.

Duffau H. Awake surgery for non-language mapping. *Neurosurgery*. 2010;66:523–529.

Kim SS, McCutcheon IE, Suki D, et al. Awake craniotomy for brain tumors near eloquent cortex: correlation of intraoperative cortical mapping with neurological outcomes in 309 consecutive patients. *Neurosurgery*. 2009;64:836–846.

B.2. What are the current symptoms and why are they important?

In order to successfully complete an awake craniotomy, the patient must be motivated to undergo the demanding procedure and able to effectively communicate with the neurosurgeon, the neurologist, and the neuroanesthesiologist. The patient must also be able to read short phrases, identify various objects, and describe pictures.

A patient who presents with some form of dysphasia may not be able to participate at all. Expressive dysphasia and global dysphasia are extreme examples, but not uncommon presentations. At times, a short course of corticosteroids will decrease the penumbral area enough that verbal testing is practical. Some patients will present greatly agitated. Although this is usually their presenting symptom, they cannot cooperate in any fashion, even with minimal commands, and other means are necessary to care for these folks.

Areas of muscular weakness or paralysis, either from the current problem or past injury, must be identified preoperatively to differentiate between postoperative worsening and new neurologic deficits. Rarely will the patient show improvement in the immediate postoperative period; however, pre-existing problems can actually be accentuated in the postoperative period.

Overall, patients who cannot communicate effectively or cooperate do not make good candidates for an awake craniotomy.

B.3. Are there anesthetic implications from current treatment drugs?

Refer to Table 18.1 once again. Many of the AEDs currently available for treating patients with seizure disorders or those secondary to a brain tumor are listed here.

Many of these drugs, such as the benzodiazepines, hydantoids, analogs, and phenytoins, can interfere with drug metabolism in the liver, requiring increased dosages of IV anesthetic agents and narcotics.

In those patients started on dexamethasone, one may encounter several related abnormalities. Potential side effects associated with corticosteroid use include, but are not limited to, increased white blood (WBC) cell count, glucose intolerance, corticosteroid "stress ulcers," corticosteroid-induced psychosis, hypertension, water and electrolyte imbalance, suppression of the hypothalamic–pituitary–adrenal axis, weight gain, and impaired wound healing.

B.4. What laboratory data are required?

Although the current practice is to minimize the number of preoperative laboratory tests obtained, several are necessary in the patient undergoing a craniotomy, awake or under general anesthesia, for tumor or epileptic foci resection.

Coagulation studies are a must. Although some tumors can have a significant amount of blood loss associated with their pathology (meningiomas), bleeding from an abnormal coagulation system into a tumor bed can pose very serious and at times life-threatening problems. Partial thromboplastin time, prothrombin time, international normalized ratio, and fibrinogen and platelet counts are routinely obtained. In patients who are or have recently taken clopidogrel bisulfate or other antiplatelet, adenosine diphosphate inhibitors, a platelet activity test might prove beneficial. Check with your local laboratory. This test requires specialized equipment and may be done only at certain times of the day; it may require some form of prenotification to the laboratory to ensure that pretesting preparation is completed before the blood sample arrives. Some AEDs may cause thrombocytopenia, but leukopenia is more common.

Electrolyte studies are necessary. This patient population can have imbalances from substances secreted by the tumor, such as atrial natriuretic factor, or secondary to drug effect, such as hyponatremia or hypokalemia. Blood glucose levels are also included and should be controlled to 120 mg per dL or less, but hypoglycemia (less than 55mg per dL) should be avoided, although this may differ among patients. Complete blood count with differential will give information about the hematocrit and white blood cell count. The differential will be normal if the WBC count is elevated from degranulation of the WBCs caused by preoperative corticosteroids. If not, an infection may be present and must be addressed. A routine urinalysis will rule out an asymptomatic urinary tract infection.

Blood type, antibody screen, and crossmatch are also required. In the case of a positive antibody screen, at least four units of crossmatched blood are recommended to be available before starting the procedure. My worst case experience was having a patient with several major antibodies present and compatible with only 1 in 10,000 blood donors. It took 4 days to find the acceptable blood and we settled for only 2 units. It was never taken out of the blood refrigerator, was not needed, and was shipped to the next destination early the following morning. Transfusion during an awake craniotomy is uncommon because these lesions are usually small. Nevertheless, if it does become necessary, you need that blood immediately, not 30 to 45 minutes from now. For a negative antibody screen, 2 units of blood readily available is acceptable.

Depending on comorbidities, an electrocardiogram (ECG) can be obtained.

B.5. What radiology data should be reviewed?

Reviewing the most recently obtained MRI or CT scans can give you a great deal of insight about the intracranial pathology. Characteristics of the tumor such as ring enhancement, cystic or lobulated nature, or variously weighted CT studies may give the neuroradiologist and neurosurgeon some insight regarding the diagnosis of the tumor as well as the location of the lesion. The location of the lesion may confirm the presenting symptoms. Vasogenic edema is readily seen, and the progress of resolution with corticosteroids is possible by reviewing a series of CT scans since presentation. Additional information can be gained, but is not always present for the smaller lesions usually associated with the awake craniotomy. A midline shift would be evidence of increased ICP, as would loss of sulci and gyri, not to mention the presence of uncal or falcine herniation (Fig. 18.5). The presence of hydrocephalous from blockage of CSF pathways is also readily seen and could be a source of increased ICP. Previous areas of stroke are usually easily visualized and need to be noted. This is a very rapidly changing field, so there should be no hesitation in calling on the neuroradiologist or neurosurgeon to point out the pathology and their major concerns. A neuroanesthesiologist can never overcommunicate with the neurosurgeon.

B.6. How do you prepare the patient for an awake craniotomy?

Many things can help prepare the patient for this very demanding procedure. The most important, though, is proper patient selection, which was alluded to earlier.

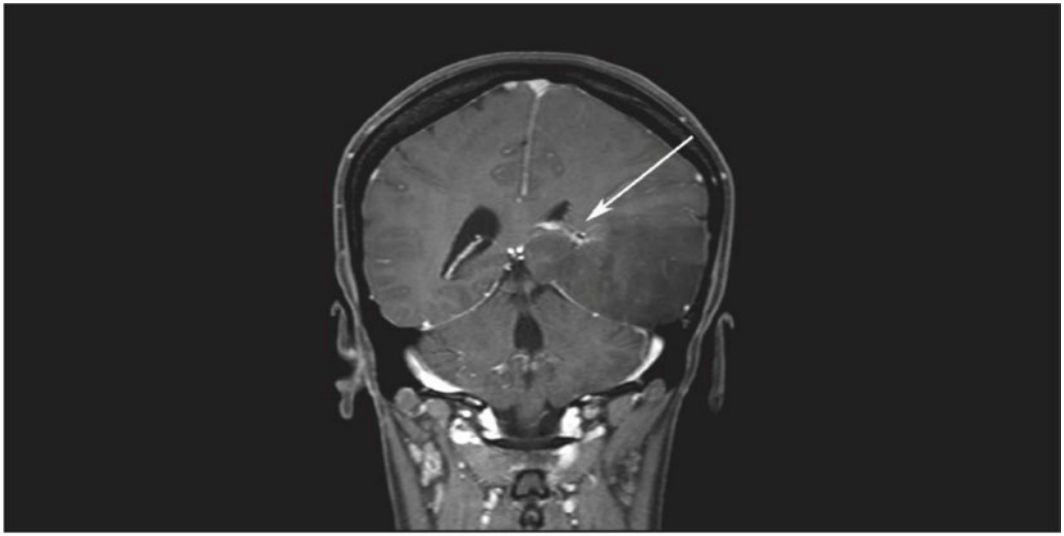

Figure 18.5 MRI scan of a 29-year-old female school teacher with a 2-week history of word-finding difficulty and no other symptoms. Note the rather significant uncal herniation (arrow). The patient underwent an uneventful left, awake craniotomy with language area mapping and was discharged to home the next day. Final pathology revealed a World Health Organization grade III anaplastic oligoastrocytoma.

A patient who cannot effectively communicate and cooperate will not do well with this procedure regardless of how precisely everything else is done.

The need for an awake craniotomy is usually first broached by the neurosurgeon during the workup. It is not at all unusual then to have a rather concerned and anxious patient arrive in the preanesthetic clinic. Ideally, the neuroanesthesiologist who will handle the case will conduct the interview, though this is frequently not the case. If not, then the neuroanesthesiologist must make every effort to see the patient well before the time to go to the operating room. In either case, a direct and detailed explanation of what will happen should proceed. Assure the patient, as often as needed, that adequate means will be taken to control any pain. Reassure the patient that he or she can ask for more medications if needed, but also discuss limitations secondary to needing the patient awake and cooperative. Discuss additional IV lines, invasive monitors if deemed necessary and why they are used, and when they will be placed.

A discussion about the anesthetic itself is essential. Usually, if patients have a good understanding of the sequence of the procedure and that they may not be exactly fully awake for the entire time they are in the operating room, they are more at ease. Describe everything in detail. This may be the first surgical procedure they have ever had and its going to be awake.

B.7. Should this patient receive premedications?

Any premedications that might affect the intraoperative ability to adequately map the cortex are contraindicated. This includes medication that might not only cause prolonged sedation, but in the case of epilepsy surgery, interfere with intraoperative intracranial electrocorticography to define the epileptic foci. In particular, benzodiazepines and barbiturates should be avoided for these reasons. Most of the time, the calm and reassuring neuroanesthesiologist is the best "premedication."

B.8. What precautions should be made for airway management?

Airway evaluation is extremely important in this patient population. The head will most likely be fixed in a three-prong head-holding device, making the ability to intubate the patient via direct laryngoscopy virtually impossible. Further limitations include the surgical drapes and the instrument table, which often extends over the patient completely. The patient is often positioned in the lateral decubitus position, making moving the patient to a flat position time consuming, if even possible at all. Patient body habitus can also make this very challenging in the nonsupine position. Obese and morbidly obese patients present exceptionally difficult challenges; edentulous patients have bone erosion of both the axilla and mandible that could make mask ventilation difficult in any position. Patients on phenytoin can have rather impressive gingival hypertrophy and associated bleeding that can interfere with intubation if required; teeth can be loose and easily displaced. All of these problems can make placement of an airway or laryngeal mask airway (LMA) difficult at best, impossible at worst. The next section suggests that the use of an LMA or even endotracheal intubation for these cases is for some the preferred method.

Having an airway cart immediately available and prepared for a fiber-optic intubation with an assorted and readily available selection of LMAs is recommended. At baseline, a nasal cannula for oxygen delivery and CO_2 measurement should be placed before starting sedation.

C. Intraoperative Management

C.1. How should this patient be monitored?

Monitoring should be in accordance with the guidelines of the American Society of Anesthesiologists. These include pulse oximetry, electrocardiography, noninvasive blood pressure monitor, capnography, and temperature measurement as a minimum.

American Society of Anesthesiologists. Standards for basic anesthetic monitoring. Available to members at http://www.ASAhq.org.

C.2. Does this patient require invasive monitoring?

In general, for an awake craniotomy, invasive blood pressure monitoring is not a requirement. Nevertheless, some circumstances might be better served with an arterial line. Blood pressure measurement with an oscillometric device can be problematic in patients with atrial fibrillation; it also overestimates both systolic and diastolic blood pressure readings in patients with stiff arteries, such as diabetics. The diabetic patient may also require frequent blood glucose measurements, and the presence of an arterial line facilitates this and avoids multiple venous blood draws in the operating room.

A central venous line (CVL) for pressure measurement is not required in the awake patient. Nevertheless, at times, venous access is so poor that one needs to be placed merely for that purpose.

Remember, the best monitoring system for this case is the awake, cooperative patient.

Van Popele NM, Bos WJW, deBeer NAM, et al. Arterial stiffness as underlying mechanism of disagreement between an oscillometric blood pressure monitor and a sphygmomanometer. *Hypertension.* 2000;36:484–488.

C.3. Can current drug therapy alter eloquent cortex mapping?

For mapping of the language areas, any drug that would cause long-lasting, deep sedation, as discussed earlier, would be contraindicated. Patients presenting with new onset of seizures associated with the new diagnosis of brain tumor may have been started on any one or several of the AEDs listed in Table 18.1. These drugs may interfere with mapping of the eloquent cortex. In patients undergoing epilepsy surgery, the surgeon has usually stopped these drugs several days in advance so as not to interfere with intraoperative electrocorticography, the placing of electrodes directly on the surface of the exposed brain. Corticosteroids and opioids would not interfere, but propofol can leave a pattern of high-frequency, high-amplitude beta activity on the electroencephalogram for at least 20 minutes, which can cloud the abnormal activity being sought and should be stopped appropriately.

C.4. Why use hypertonic fluids during a craniotomy?

The intact brain, primarily the BBB, acts as an osmometer. Water will freely cross this semipermeable membrane in response to various osmotic pressures created by dissolved solutes until there is an equal water pressure across the membrane. This is a function of the number of osmotically active, dissolved solutes (osmoles) present in a solution: The greater the number of osmoles, the greater is the osmolarity or osmotic activity of the solution. At times, this is also called the *osmolality*. This term describes the same principle, but does have several differences. *Osmolarity* is defined as osmoles per liter of fluid and is a calculated value. Osmolality is one of the four colligative properties of a solution. It is defined as osmoles per kilogram of fluid and is a measured value, usually by a freezing point depression method.

Table 18.2 lists several commonly used IV fluids and compares their osmolarity and osmolality. The osmolality is lower secondary to the presence of undissolved solutes in the solution. When solutes are given IV, the intact BBB prevents the solutes from crossing into the brain, thus sequestering the particles to the intracranial intravascular space and creating a high osmotic pressure. The result is a water concentration in the vessels that is less than that in the brain, with resultant movement of water from the brain into the vascular space. This reduces brain bulk, which may provide better visualization of the tumor by the surgeon and hopefully decreases the need to apply retractors to the brain surface to enhance visualization. This in turn may help

Table 18.2 Osmotic Values of Common Intravenous Fluids

FLUID	OSMOLARITY (mOsm/L)	OSMOLALITY (mOsm/kg)
Water	0	0
D_5W	252	259
NS	308	282
LR	273	250
3% Saline	1,027	921
6% Hetastarch	310	307
20% Mannitol	1,098	1,280
5% Albumin	290	283
Normosol–R	294	281
D_5W/0.2 NaCl	325	321

D_5W, 5% dextrose in water; NS, normal saline; LR, lactated Ringer's solution; D_5W/0.2 NaCl, 5% dextrose and 0.2% sodium chloride.

decrease ischemic injury to the brain directly under the retractors. It also decreases ICP in the intact brain. Intravascular proteins create a much smaller oncotic pressure in the intracranial vasculature than do the dissolved solutes, secondary to the intact BBB, and play a lesser role than they do in the systemic circulation, where they are the primary determinant of fluid moving extravascular to intravascular.

Cerebral blood flow, cerebrospinal fluid, and brain metabolism. In: Guyton AC, Hall JE, eds. *Textbook of Medical Physiology*. 12th ed. Philadelphia: Saunder; 2011:743–752.

Rusa R, Zarnow MH. Fluid management during craniotomy. In: Cottrell JE, Young WL, eds. *Cottrell and Young's Neuroanesthesia*. 5th ed. Philadelphia: Mosby Elsevier; 2010:147–160.

C.5. What intravenous fluids (IVFs) are recommended?

Commonly used IVFs during craniotomy, awake or under general anesthesia, are 0.9% saline, 3% saline, lactated Ringer's solution, 20% mannitol, and 5% albumin.

Normal plasma osmolality is 285 to 295 mOsm per kg. Therefore, any solution with a higher osmolality could act to pull water from the brain. The exception to this is any solution containing 5% dextrose. These solutions have an effective osmolality 259 mOsm less than the measured osmolality because glucose (osmolality 259 mOsm per kg) is rapidly metabolized by the brain. D_5W thus has an effective osmolality of zero and D_5W/0.2 NaCl an effective osmolality of 62 mOsm per kg as examples. These dextrose-containing solutions would present a very high concentration of free water within the intracranial intravascular space and result in water movement into the brain causing an increase in ICP or brain bulk.

It is now well accepted that hyperglycemia before or during an episode of cerebral ischemia worsens outcomes. The mechanism is not clear. One hypothesis is that during a hyperglycemic episode, the increased level of intraparenchymal glucose reacts with substances for lactic acid production during the ischemic period, which is thought to have a negative effect leading to neuronal death. This being said, solutions containing D_5 are not routinely used during intracranial surgery.

Twenty percent mannitol is the most widely used IVF for treatment of elevated ICP. It also acts to decrease CSF production and acts as a scavenger of oxygen free radicals. Mannitol should be given IV over 10 to 15 minutes to prevent a sudden exposure of the cerebral circulation to extreme hyperosmolality (mannitol has an osmolality of 1280 mOsm per kg), which could lead to a vasodilatory effect with resultant increased CBV, possible brain engorgement, and increased ICP. Increased urine output secondary to this diuresis should be replaced with normal saline. The usual mannitol dose is 0.25 to 1 g per kg.

Hypertonic saline comes in a range of concentrations, with 3% probably being the most commonly used during intracranial surgery. A recent study has shown no difference between equiosmolar mannitol and hypertonic saline infusions for providing brain relaxation.

Normal saline has traditionally been the fluid of choice for intracranial procedures and is used to cover fluid requirements and replace blood loss until red blood cells are required. A drawback to its use is that a hyperchloremic, hypokalemic metabolic acidosis can occur when large volumes are given. This can mask any other form of acidosis and cloud the diagnostic picture. Lactated Ringer's solution (osmolality 250 mOsm per kg) would not theoretically, based on the prior discussion, be an ideal replacement for blood loss, insensible loss, or third-space losses. Nevertheless, it is being used in many centers without problems. Some authors have suggested alternating normal saline and lactated Ringer's solution one after the other in the setting of large-volume administration.

The crystalloid versus colloid debate seems to be never ending and is usually centered on head injury. Colloid, in the form of 5% or 25% albumin is rarely, if ever, needed in an awake craniotomy.

Drummond JC, Patel PM. Neurosurgical anesthesia. In: Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:2045–2087.

Myburgh J, Cooper J, Finfer S, et al. Saline or albumin for fluid resuscitation in patients with traumatic brain injury. *N Engl J Med*. 2007;357:874–884.

Rozet I, Tontisirin N, Muangmam S, et al. Effect of equiosmolar solutions of mannitol versus hypertonic saline on intraoperative brain relaxation and electrolyte balance. *Anesthesiology*. 2007;107:697–704.

Suarez JI, Shannon I, Zaidat OO. Effect of human albumin administration on clinical outcome and hospital cost in patients with subarachnoid hemorrhage. *J Neurosurgery*. 2004;100:585–590.

C.6. Would a lumbar drain for CSF removal benefit this patient?

The lesions in the eloquent cortex are usually small, so a lumbar drain is not indicated. Historically, neurosurgeons have placed a lumbar drain before the start of the surgery to allow CSF to be drained slowly, usually 10 mL per hour, to decrease brain bulk. This might have been placed in an "open" position when the time came to open the dura, allowing for maximal brain relaxation and visualization in addition to preventing any intracranial contents from herniating through the craniotomy site proper.

Bruder N, Ravussin PA. Supratentorial masses: Anesthetic considerations. In: Cottrell JE, Young WL, eds. *Cottrell and Young's Neuroanesthesia*. 5th ed. Philadelphia: Mosby Elsevier; 2010:184–202.

C.7. Venous air embolism (VAE): Is it a concern in this case?

Venous air embolism is the entrainment of air into open, noncollapsible vascular structures located above the level of the heart. Therefore, the short answer is yes, because the level of the surgical site meets this definition.

VAE is usually associated with posterior fossa craniotomies and cervical spine surgery in the sitting position. Fatal VAE has been described with as little as 3 to 5 cm of surgical site elevation above the heart during lumbar spinal surgery, with the patients supported on a four-poster support device in the prone position.

In this case, the tumors are usually small and within the cortex, and the patient is either supine or in a nearly horizontal lateral decubitus position. Parasagittal and falcine meningiomas encroaching on the posterior portion of the sagittal sinus are the most common situations for VAE development. Fortunately, the eloquent cortical areas are not in this location. Nonetheless, VAE has been reported after pin head-holder placement and after craniotomy, but before dural opening. This implies that free air can be entrained through the diploic space of the skull unless adequately sealed during the cranial opening. This is usually done with wax. Therefore, as stated earlier, VAE is a possibility during an awake craniotomy.

Although transesophageal echocardiography is the most sensitive means of detecting VAE, it is impractical in the setting of the awake craniotomy. The precordial Doppler device is the monitor of choice for this particular scenario if the head will be elevated above the level of the heart. When placed in the right or left parasternal region between the third and fourth ribs, Doppler has a high detection rate for VAE. Often, the awake patient may experience an episode of paroxysmal coughing with entrainment of air. The best chance of aspirating a VAE is through a properly placed, multiorificed central line that is positioned 2 cm below the superior vena caval–atrial junction. This is accomplished by using intravascular ECG. Lead two is observed while the electrode of the CVL is attached to the leg lead. An equibiphasic P wave indicates that the tip of the catheter is in the midatrial position.

Treatment for VAE is supportive. If venous air embolism is suspected, the surgeon must be immediately informed and the surgical field flooded with water to help prevent further air entrainment. Jugular compression and lowering the head are also maneuvers to help stop air entrainment. If it is present, an attempt should be made to aspirate air through the CVL simultaneously with the surgeon addressing the surgical field. Vasopressors or inotropes as needed are given to support hemodynamics, and cardiopulmonary resuscitation initiated if all else fails.

Albin MS, Ritter RR, Pruett CE. Venous air embolism during lumbar laminectomy in the prone position: report of three cases. *Anesth Analg*. 1991;73:346–349.

Drummond JC, Patel PM. Neurosurgical anesthesia. In: Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:2045–2087.

Jellish WS, Murdoch J, Leonetti JP. Perioperative management of complex skull base surgery: the anesthesiologist's point of view. *Neurosurg Focus*. 2002;12:1–7.

C.8. How is the eloquent cortex mapped?

Before the start of the case, the neurologist will go over the intraoperative testing procedure with the patient. This usually consists of various confrontational type testing in which the patient may be asked to simply count. At other times, the patient may be asked to name items on a card preceded with the phrase "that is a . . . ." Patients are sometimes asked to do simple math problems. It is important to realize that a patient who speaks multiple languages may need to have each of those languages tested separately. Not all learned languages are "laid down" in the same cortical area. This requires extensive preoperative planning to have the needed interpreters available to help with this testing.

Once the craniotomy is completed, the dura opened, and the patient awakened, testing can begin. The tumor surface is often visible and helps guide the surgeon as to where to start the mapping. A handheld wand with two probes, separated by 5 mm, is gently placed on the brain surface about 2 cm from the tumor edge. This is connected to a constant-current, biphasic stimulator. Our neurologists usually stimulate for 2 to 5 seconds with a frequency of 50 Hz and a pulse width of 200 ms. Responses are usually noted with a stimulus power range of 4 to 6 mA. After each test, the surgeon moves the wand freely to other areas of the cortex, repeating this procedure until satisfied that functional areas of the cortex have been localized and marked and that an area of negative mapping has been identified through which the tumor or epileptic foci can be resected.

In the case of seizure focus resection, there are no visible signs to follow. Often, the areas of eloquent cortex in danger will have been mapped out by MEG. This is a noninvasive technique for mapping brain activity by recording the magnetic fields produced by the electrical currents of the brain. These studies can then be "laid over" an MRI study and appear as colored squares representing areas of the eloquent cortex tested and can be used for tumor or epilepsy surgery to help identify the functional areas. Mapping can then start outside of these designated areas looking, again, for a quiet area.

Moore TA, Markert JM, Knowlton RC. Dexmedetomidine as a rescue drug during awake craniotomy for cortical mapping and tumor resection. *Anesth Analg*. 2006;102:1556–1558.

C.9. How are intraoperative seizures treated?

Intraoperative seizures can be either the baseline type, for which the patient presented, or they can be caused by the cortical surface stimulation used to map the cortex.

The surgeon usually will not stimulate the same area more than two consecutive times, to avoid this complication. If a seizure should occur, it usually will take the form of the patient no longer answering any questions, but maintaining their airway, and at times maybe a slow moaning sound will be made. This usually responds rapidly to the application of a cold irrigation solution, usually lactated Ringer's solution, to the cortex by the surgeon. If this fails, small doses of propofol, 10 to 20 mg, will usually suffice to stop the seizure.

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C.10. How will you conduct this anesthetic?

The conduct of this type of anesthetic actually begins long before the patient ever enters the operating room. As discussed earlier, the patient must be very motivated for this experience to be successful. The patient must realize fully that this is a lengthy procedure and 4 to 6 hours is not an unusual expectation for being in the operating room. The patient's family must also be involved and have the same understanding. Most important is a motivated and experienced neurosurgeon and neurologist. Each must realize that time is of the essence and the procedures must be completed as quickly as is safely possible.

The neurosurgeon will be the first person to suggest or inform the patient that this form of surgery is necessary to preserve their language or motor-sensory function.

Ideally, the neurosurgeon and the neuroanesthesiologist have a successful history of performing this procedure. They have developed a technique that has allowed them to have an awake, cooperative patient when the time comes for cortical or subcortical mapping and resection.

In the operating room, before patient arrival, several steps are taken to make the patient as comfortable as possible during this long and demanding procedure. A full-length gel pad is placed on the operating room table under the sheets and the room temperature is set at 70° F or higher. Additional gel pads and foam sheets are available as needed, as well as warm blankets.

Following the preoperative visit and IV line placement, the patient is brought to the operating room. As previously discussed, premedications that interfere with the patient's ability to cooperate and follow instructions are contraindicated. Standard intraoperative monitors are placed as described earlier, and a carbon dioxide monitoring nasal oxygen cannula is placed.

The literature is replete with reports of anesthetic techniques for the awake craniotomy. The common theme is a triphasic "asleep-awake-asleep" technique. The approach is as varied as the number of neuroanesthesiologists who perform these procedures.

Some of these techniques use intubation of the trachea and the use of potent inhalational agents until approximately 20 to 30 minutes before cortex mapping when the anesthetic is discontinued and the patient extubated. Others describe the use of an LMA in the same fashion. The use of propofol, fentanyl, remifentanil, dexmedetomidine, and various combinations of these drugs have been described as being added to these approaches as a means of transitioning the patient from a general anesthetic to the awake state for mapping and surgery within the eloquent cortex. The use of total intravenous anesthesia using the same drugs has also been described with the airway controlled by an LMA with controlled or spontaneous breathing or an unprotected airway with spontaneous respirations.

The literature describes cases in which similar, but not identical, approaches for mapping or other tasking has been successful for one group and not for another. This can lead to tremendous frustration in trying to decide how to administer this

anesthetic. Many times, the technique is institutionally defined and has worked well for many years.

One of the most important things is to fully understand the pharmacology of the anesthetic regimen chosen.

Our institution uses a triphasic total intravenous anesthesia technique with spontaneous breathing without LMA or tracheal intubation. After standard monitors are placed, two separate infusions are started. Dexmedetomidine is started at 0.35 μg/kg/hr and propofol is started at 75 μg/kg/min. These drugs are titrated as needed to achieve a sedated, yet spontaneously breathing patient. When the patient no longer responds to name call, a Foley catheter, additional IV lines, and an arterial line, as deemed necessary, are placed. Small bolus doses of propofol 10 to 20 mg are given depending on patient response to these procedures.

A loading dose of dexmedetomidine is given at the discretion of the attending neuroanesthesiologist. The recommended administration is 1 μg per kg over 10 minutes, and then the maintenance infusion is started. Several reports have described levels of persistent bradycardia and hypotension with this approach versus starting the infusion without the loading dose. We prefer the dexmedetomidine and propofol combination because it provides good sedation, anxiolysis, and some amnesia without causing respiratory depression.

The anesthesiologist must realize from the beginning that the success of this procedure lies almost entirely with the precision and adequacy of the scalp blocks performed by the anesthesiologist or the neurosurgeon. No amount of sedation will compensate for poorly performed blocks. In our institution, the scalp block addresses the supratrochlear, supraorbital, zygomaticotemporal, auriculotemporal, and greater auricular and the lesser and greater occipital nerves. A combination of equal volumes of 1% lidocaine with epinephrine 1:100,000 and 0.25% bupivacaine with epinephrine 1:200,000 is used as the local anesthetic solution. The mixing of local anesthetic solutions to obtain a solution for injection has been performed in an attempt to obtain an anesthetic solution that will have a rapid onset and longer duration than either of the component solutions separately. In reality, no convincing data support this practice. The use of ropivacaine singularly for the same purpose is described numerous times in the literature. Following the individual nerve blocks, an intradermal ring of the local anesthetic solution is placed around the operative side of the scalp. Each pin site for the pin head-holder device is injected, as is the surgical incision site, by the surgeon, after the patient is prepped and draped.

The dexmedetomidine and propofol infusions are continued as the cranial opening proceeds. When the surgeon has placed the final burr hole, the propofol is turned off and the dexmedetomidine is turned down to 0.2 μg/kg/hr. The cranial opening continues, and approximately 15 to 20 minutes later, the patient is awake and conversant. The neurosurgeon and neurologist begin the mapping process, which can take several hours, but on average, in our institution, this is accomplished in 50 to 60 minutes. The dexmedetomidine is continued at 0.2 μg/kg/hr throughput the mapping process. When satisfied that areas of the eloquent cortex adjacent to the tumor have been localized and an area of negative mapping have been demonstrated, the surgeon proceeds with tumor resection. If the patient is resting comfortably, we do not make any changes in the anesthetic. If they ask to be more sedated, the dexmedetomidine is increased to 0.35 μg/kg/hr; this usually keeps the patient comfortable for the remainder of the procedure. From time-to-time, the surgeon may ask to remap certain areas. The dexmedetomidine is again lowered to 0.2 μg/kg/hr, if needed, and the remapping with the neurologist commences. The dexmedetomidine is stopped with skin stapling. The pin head-holder is removed, dressings are placed, and preparations are made for leaving the operating room and transferring to the neurosurgery intensive care unit.

A transport monitor capable of providing pulse oximetry, blood pressure measurements, and ECG tracing is attached to the patient and nasal cannula oxygen is continued during the transport to the neurosurgery intensive care unit.

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D. Postoperative Management

D.1. What are the major concerns following craniotomy?

Several problems can occur in the immediate postoperative period following craniotomy. In general, the patient is transported to the neurosurgery intensive care unit and monitored as previously described. The head of the bed is usually elevated 20 to 30 degrees to maximize cerebral venous drainage.

Emergence hypertension is not uncommon in the perioperative period, even after an awake craniotomy. The incidence of postcraniotomy hypertension has been reported to be 57%. In this series of 11,214 craniotomies, perioperative systemic hypertension was associated with postoperative intracranial hematomas with resultant increased mortality and increased length of hospital stay. Other possible causes are pain, hypercapnia, and shivering. Eighty-five percent of postoperative intracranial hematomas become evident within 6 hours of surgery and usually present as a progressive decrease in the level of consciousness. Up to 17% of these hematomas can present at sites remote to the surgical site. Aggressive efforts at controlling this hypertension are required to prevent possible devastating complications such as bleeding into the tumor bed, requiring a second surgical procedure to evacuate that clot.

If not contraindicated, bolus doses of labetalol 5 to 10 mg IV usually control this quite well. Nevertheless, at times, persistent hypertension, without signs of intracranial hypertension, may require additional treatment. Hydralazine 5 to 10 mg IV, an infusion of nicardipine 5 to 15 mg per hour, an infusion of sodium nitroprusside, or nitroglycerin are possible choices. A combination of enalapril and labetalol versus nicardipine alone has been reported, with little difference in the ability to control emergence hypertension.

Acute pain control is essential in the postoperative period. Not only are the patients more comfortable with adequate pain relief, but this also helps control postoperative hypertension and decreases the possibility of intracranial hematomas. Pain following craniotomy has probably been vastly understated secondary to concern about respiratory depression and sedation, as well as the traditional thought that

craniotomies are less painful than other operations. The incidence of postcraniotomy pain may be as high as 70%.

Codeine sulfate has traditionally been the opioid of choice for postcraniotomy pain control because it does not mask pupillary signs and it has a ceiling to its respiratory depressant effects. Nevertheless, it is only about half as potent as morphine sulfate and causes profound hypotension if given IV, leaving the oral, rectal, or intramuscular injection route for administration.

In the immediate postoperative period, almost all pain control medications are given IV. Morphine sulfate patient-controlled analgesia has been reported with good results and without incidence of respiratory depression or need for reintubation. This regimen consists of morphine 1.5 mg with a lockout period of 8 minutes and a total dose not to exceed 40 mg in 4 hours.

Nonsteroidal anti-inflammatory drugs have been associated with postoperative intracranial hematoma formation. Administration of antiplatelet agents (aspirin and nonsteroidal anti-inflammatory drug) was the most commonly associated risk factor. Therefore, this class of pain control medications should be avoided in the immediate postoperative period.

Postoperative nausea and vomiting is common following craniotomies and can cause hypertension and an increase in ICP. Infratentorial surgery, female gender, and a young age are associated risk factors. Ondansetron 1 to 4 mg IV can provide effective treatment.

Seizures can occur following intracranial tumor resections and can cause serious complications such as secondary intracranial bleeding, hypoxia, and possibly aspiration. An intracranial mass, such as a hematoma (Fig. 18.6), should be suspected if

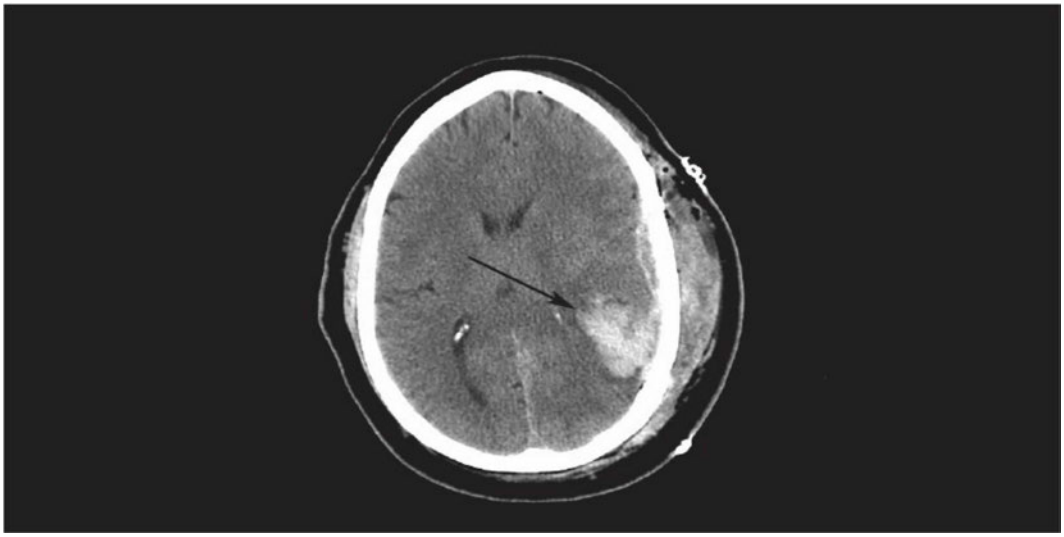

Figure 18.6 CT scan of a 73-year-old man who underwent an uneventful left, awake craniotomy with motor and language area mapping. On postoperative day 2, he suffered a generalized tonic–clonic seizure and was extremely slow to awaken. CT scan revealed the presence of a large intracranial hematoma (*arrow*) in the operative site requiring return to the operating room for evacuation. Also note the small epidural and subglial hematomas. Coagulation studies were normal. The patient was placed on antiepileptic drugs and was doing well on follow-up visits without further seizure activity. Antiepileptic drugs were successfully weaned over several weeks. Final pathology revealed glioblastoma multiforme.

the patient does not regain consciousness within a short period after the seizure has ceased. Small doses of midazolam, 1 to 2 mg, or other benzodiazepines can treat this problem effectively without compromising the airway.

Increased ICP commonly occurs after intracranial surgery, with the most common finding on CT scan being brain edema. Maximum pressures are usually recorded within 16 hours of surgery. Associated risk factors are glioblastoma resection and surgery lasting more than 6 hours. Continuing corticosteroids, dexamethasone 6 to 10 mg every 6 hours, usually controls this problem.

Peripheral nerve injuries are uncommon after awake craniotomy because patient comfort or discomfort can easily be assessed, and minor movements made if needed. We have experienced several episodes of blister formation along the down side of a morbidly obese patient's upper leg after about 5 hours in the lateral decubitus position in spite of the use of gel pads beneath the thigh. Supportive treatment was provided, and this was resolved by the first postoperative follow-up visit.

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CHAPTER 19

Head Injury

EUGENE S. FU, JONATHAN JAGID, AND LEO T. HARRIS III

A 22-YEAR-OLD WOMAN

presented to the trauma center after sustaining multiple gunshot wounds on the head and face. On admission, the patient had a Glasgow Coma Scale (GCS) of 8 and vital signs were blood pressure, 134/72 mm Hg; heart rate, 138 beats per minute; respiratory rate, 20 breaths per minute; and oxygen saturation, 100%. The patient developed a coagulopathy as hemoglobin dropped from 12 g per dL to 5 g per dL, for which the patient was transfused with packed red blood cells and fresh frozen plasma. Eventually, recombinant human factor VIIa was given subcutaneously to correct the coagulopathy in preparation for surgical intervention. Head computed tomography (CT) scan showed an expanding intracerebral hematoma in the right frontal lobe (Fig. 19.1). The patient was taken to the operating room for a right craniectomy for evacuation of the anterior frontal lobe hematoma and debridement of bullet and bone fragments. Postoperatively, the patient underwent a cerebral angiography revealing a traumatic ophthalmic artery aneurysm (Fig. 19.2). On postoperative day 1, the patient developed polyuria and hypernatremia, indicative of diabetes insipidus (DI).

A. Pathophysiology and Differential Diagnosis

1. What types of intracranial injuries are most likely to have occurred in this patient?
2. What is the difference between primary and secondary injury? What factors contribute to secondary injury?
3. What are the risks and benefits of administering mannitol?
4. What is the effect of hyperglycemia on neurologic outcome following head trauma?
5. What alterations in sodium and potassium balance can occur in patients with head injury?
6. In addition to sodium and potassium, what other electrolyte abnormalities can be present after head trauma?

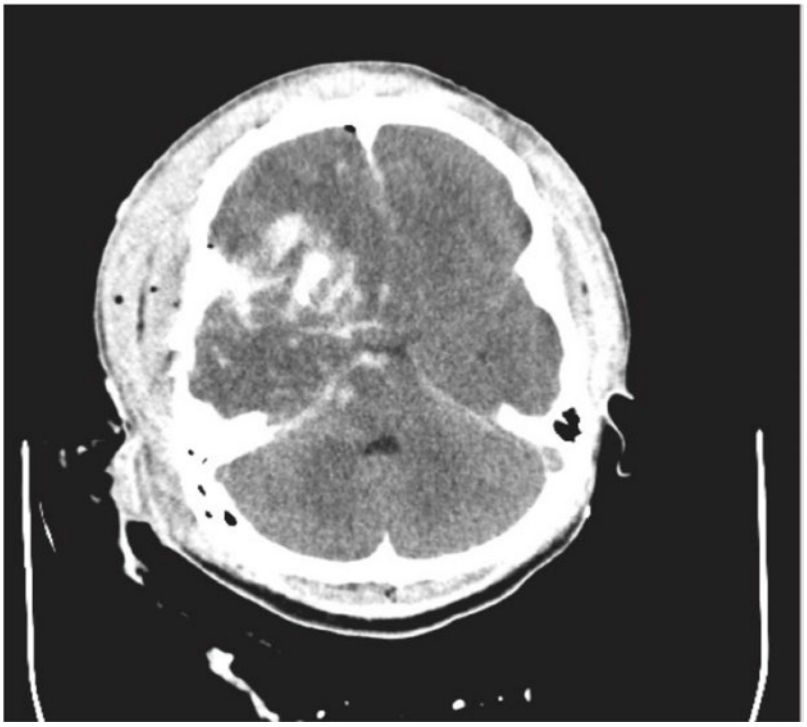

Figure 19.1 Head computer tomography scan showing expansion of intracerebral hematoma after gunshot wound.

7. What are the neuroprotective effects of administering magnesium?
8. What role do gender and female sex hormones have in the pathophysiology of traumatic brain injury (TBI)?
9. What is the role of decompressive craniectomy as a treatment option for intracranial pressure (ICP) control after head injury?
10. Do genetic factors play a role in the outcome after head injury?

B. Preoperative Evaluation and Preparation

1. What is the GCS? What is the significance of a GCS of 8 in this patient?
2. In addition to the GCS, what other assessments can be done to evaluate neurologic function?
3. What is the role of CT scanning in the initial evaluation of the patient with head injury? What management options can be done in patients whose neurologic condition is deteriorating before obtaining a CT scan?
4. What is the role of ICP monitoring in the management of head injury?
5. How can you clear this patient's cervical spine?
6. What are the benefits of early endotracheal intubation in this patient?
7. What is your plan for airway management in this patient? How would it change if the patient were combative? How would it change if the patient had facial fractures with significant swelling of the head and neck?

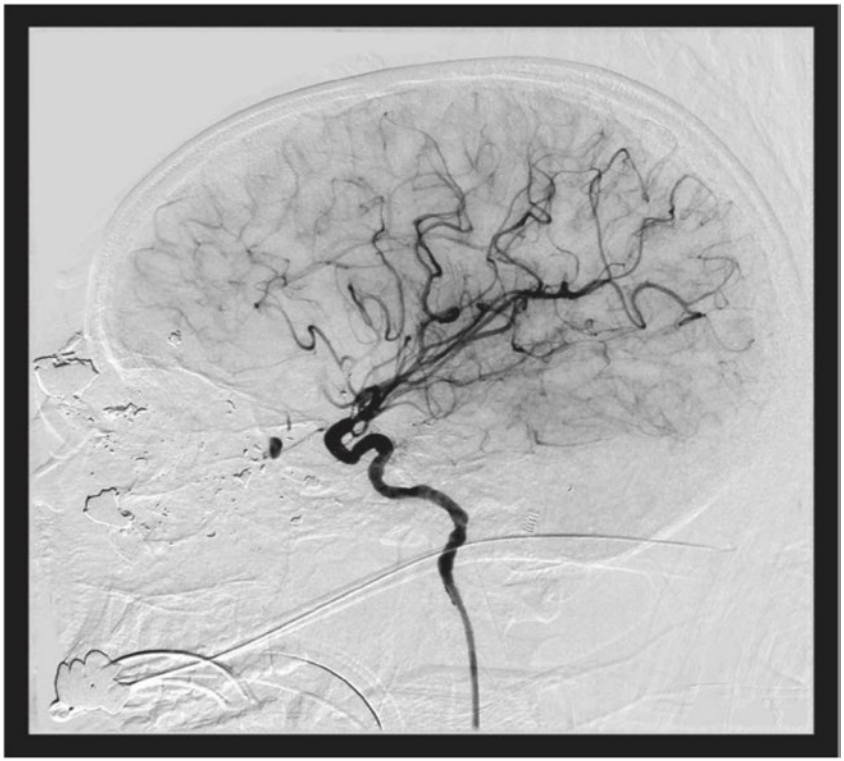

Figure 19.2 Cerebral angiogram showing an ophthalmic artery aneurysm.

8. What are the effects of succinylcholine on ICP? What is the significance of the effect, if any?
9. What coagulation abnormalities are present after TBI? What treatment modalities can be used to provide hemostasis and reduce intracranial hematoma expansion?

C. Intraoperative Management

1. What is appropriate hemodynamic monitoring during CT scanning and during craniotomy for evacuation of a subdural hematoma?
2. Should hyperventilation be used in this patient?
3. What are the implications of arterial hypertension in patients with head injury? How should blood pressure be managed?
4. What should be done about intravenous fluid replacement? Should corticosteroids be given empirically?
5. Should hypertonic saline be administered to this patient? How is hypertonic saline administered?
6. The patient underwent a craniectomy for evacuation of a frontal intracerebral hematoma. Should some anesthetic agents be avoided in this situation? Which ones? What agents might be preferred in this situation?
7. Should hypothermia be employed in this patient?

D. Postoperative Neurointensive Care Management

1. What are the postoperative ventilation considerations in this patient?
2. What specific measures should be used to control the patient's ICP? What type of monitoring devices can be used to monitor ICP?
3. What is neurogenic pulmonary edema? Would you avoid positive end-expiratory pressure (PEEP) in a patient with increased ICP?
4. What is the role of antiseizure prophylaxis in the perioperative management of head trauma?
5. How can cerebral oxygenation monitoring be used in the clinical management of TBI?
6. What methods can be used in the neurointensive care unit to prevent hyperthermia?

A. Pathophysiology and Differential Diagnosis

A.1. What types of intracranial injuries are most likely to have occurred in this patient?

The leading causes of traumatic brain injury (TBI) include falls, motor vehicle collisions, and assaults; and blasts are a leading cause of TBI in active military personnel. In a patient without obvious signs of localizing neurologic deficits, the most probable intracranial injury is cerebral contusion. This is usually a diffuse or multifocal process that results in disruption of the blood–brain barrier, causing widespread brain swelling as a result of edema. The diagnosis can be made with certainty only after ruling out other focal injuries, such as intracranial hematoma. Traumatic intracranial hematomas include epidural, subdural, and intracerebral hematomas. The clinical hallmark signifying a mass lesion is the presence of generalized elevated ICP in conjunction with focal deficits. Interestingly, most patients who were able to talk and then deteriorate into a coma had a mass lesion requiring surgery—indicating the importance of quickly diagnosing mass lesions with CT scanning. In fact, clinicians are in the process of determining how the magnitude of elevations in ICP correlate with radiologic measurements, including ventricular size, hematoma size, grade of hemorrhage, and extent of herniation.

Epidural hematomas, located between the skull and dura, are almost always caused by skull fractures. Most epidural hematomas occur in the temporoparietal region as skull fractures lacerate the middle meningeal artery. Consequently, arterial epidural hematomas can rapidly expand, constituting a true neurosurgical emergency. The classic presentation of an epidural hematoma is a patient who presents with loss of consciousness then regains consciousness only to deteriorate into coma, with a fixed dilated pupil ipsilateral and contralateral hemiparesis because of the rapidly expanding hematoma. Subdural hematomas are located between the inner surface of the dura mater and the pial surface of the brain. In contrast to epidural hematomas, subdural hematomas are caused by lacerations of the venous sinuses (e.g., lateral sinus or sagittal sinus) or cortical vasculature and tend to develop more insidiously.

Intracerebral hematomas are collections of blood ranging from petechial hemorrhages to large collections usually in the temporal or frontal lobes. Some lesions are pure hematomas or hemorrhagic contusions. Often, these hemorrhagic areas can be managed medically with serial CT scans. Indications for surgical evacuation of intracerebral hematomas include rapid mental deterioration, mass effect, and marked intractable elevations in ICP. Gunshot wounds to the head are often accompanied by intracerebral or subdural hematoma combined with the added challenge of vascular injury from bullet or bone fragments. Penetrating head injury carries the unique long-term complications of seizure, infection (abscess or empyema), and post-traumatic aneurysm. The goals of surgery include debridement of the wound with

evacuation of mass occupying lesions and retrieval of easily accessible bullet and bone fragments in the salvageable patient.

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A.2. What is the difference between primary and secondary injury? What factors contribute to secondary injury?

Primary injury represents neurologic damage that occurs at the time of impact. Secondary injury is the consequence of ischemic insults to the brain that occur subsequent to the primary injury. Prevention of further hypoxemia and hypotension are the mainstay of managing patients with head injury. Pathophysiologic processes contributing to secondary injury include (1) alterations in the balance between cerebral blood flow and metabolism, (2) disruption of cerebral autoregulation, (3) loss of cerebral vascular reactivity to carbon dioxide, and (4) cytotoxic vasogenic fluid accumulation leading to brain swelling.

Unfortunately, many patients with severe head trauma arrive to the hospital after having episodes of hypotension and hypoxemia. Improvement in outcomes depends on trauma centers having emergency teams that provide rapid treatment in the field and direct transport to the hospital. Initial management entails oxygenation by early intubation and maintenance of cerebral perfusion pressure (CPP) with rapid resuscitation to treat hemorrhagic or hypovolemic shock. The difficulty with fluid administration is that brain swelling increases ICP and increases the threshold of the mean arterial blood pressure necessary to prevent cerebral ischemia. Elevation in ICP, which heralds cerebral herniation, leads to further brain damage and increased morbidity. The use of ICP monitoring has been important in decreasing secondary injury as a means to quantify and treat cerebral hypoperfusion. Improved outcome in patients with severe head trauma has been attributed to the approach of "squeezing oxygenated blood through a swollen brain."

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A.3. What are the risks and benefits of administering mannitol?

Mannitol is currently the osmotic diuretic of choice and is initially given as a bolus of 0.25 to 1 g per kg. It reduces ICP after 15 minutes, and its effects typically last for 2 to 6 hours. Mannitol, for the management of intracranial hypertension, should be given as a bolus and *not* as a continuous infusion. Therapeutic effects of mannitol include initial improvements in red blood cell rheology and therefore blood flow and oxygen delivery to the brain, as well as delayed osmotic water withdrawal from the brain into the circulating blood volume. There is also weak evidence that concomitant use of loop diuretics, such as furosemide, result in a greater and more sustained decrease in ICP compared to mannitol use alone. Indications for administering mannitol before ICP monitoring include transtentorial herniation and progressive neurologic deterioration. Clinical effects seem to peak when serum osmolarity is kept between 300 and 320 mOsm, and elevations beyond 320 mOsm can result in renal failure. Some authors advocate the use of hypertonic saline, but evidence does not support a superior effect in TBI.

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A.4. What is the effect of hyperglycemia on neurologic outcome following head trauma?

The release of catecholamines and hyperglycemia are manifestations of the stress response to severe head injury. Patients with severe head injury have higher blood glucose levels compared with patients with moderate and minor injury. Postoperative glucose levels above 200 mg per dL have been associated with a worse neurologic outcome. Early hyperglycemia is a significant indicator of severity of injury and a predictor of outcome. Nevertheless, hyperglycemia should be treated aggressively, especially when the risk of cerebral ischemia is present. Elevated plasma glucose levels provide a substrate for anaerobic metabolism, allowing increased production of lactate during ischemia. The approach to glucose control in patients with TBI is subject to debate because the downsides of aggressive therapy are hypoglycemia and cerebral glucopenia. In one study, intense insulin therapy, with the goal of maintaining blood glucose levels at 80 to 100 mg per dL, was associated with increased microdialysis levels of glutamate, which is a marker for cellular distress. Other studies have suggested that less restrictive glucose control may be as efficacious in patients with critical neurologic illness. (Also see Chapter 16, section C.8.)

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A.5. What alterations in sodium and potassium balance can occur in patients with head injury?

Neurologically injured patients are at risk for electrolyte imbalance. Perioperative fluid administration, mannitol administration, syndrome of inappropriate antidiuretic hormone secretion (SIADH), and cerebral salt wasting syndromes are potential causes of hyponatremia. Severe hyponatremia (Na less than 120 mEq/L) may be associated with cerebral edema and seizures. The correction of hyponatremia must be gradual to avoid precipitating central pontine myelinolysis. Hypernatremia can occur as a result of enteral tube feedings, diuresis with mannitol, and DI. Basilar skull fractures may predispose to the development of DI as a consequence of shearing of the pituitary stalk. Treatment of DI entails administration of 1-deamino-8-D-arginine-vasopressin (DDAVP) in conjunction with hypo-osmolar fluids. Patients with partial

DI may respond to other agents such as chlorpropamide, clofibrate, and thiazide diuretics, which will stimulate the release of antidiuretic hormone.

Hypokalemia may result from potassium loss secondary to polyuresis in association with diuretic administration and high urine output states such as SIADH and cerebral salt wasting syndrome. Concurrent hypomagnesemia, as seen with alcoholic and diabetic patients, can aggravate hypokalemia. The loss of cellular magnesium depletes intracellular potassium, making hypokalemia more difficult to treat if magnesium supplementation is not given. In addition, serum potassium levels may decrease despite normal total body stores. Common causes of intracellular shifts of potassium include hyperventilation and insulin administration.

Polderman KH, Bloemers FW, Peerdeman SM, et al. Hypomagnesemia and hypophosphatemia at admission in patients with severe head injury. *Crit Care Med*. 2000;28:2022–2025.

Prough DS. *Update on CNS Injury: Fluid and Metabolic Management of the Neurosurgical Patient. ASA Annual Refresher Course Lectures*. Park Ridge, IL: American Society of Anesthesiologists; 2008:331.

A.6. In addition to sodium and potassium, what other electrolyte abnormalities can be present after head trauma?

Potassium and sodium levels are routinely checked perioperatively. However, magnesium and phosphate levels are not routinely ordered, so low levels of these electrolytes are more likely to remain undetected. Hypomagnesemia has been associated with cardiac arrhythmia such as torsades de pointes, sudden death, seizures, and neuromuscular irritability. Hypophosphatemia has been associated with weakness of the respiratory muscles and respiratory infections.

Polderman KH, Bloemers FW, Peerdeman SM, et al. Hypomagnesemia and hypophosphatemia at admission in patients with severe head injury. *Crit Care Med*. 2000;28:2022–2025.

A.7. What are the neuroprotective effects of administering magnesium?

Magnesium homeostasis is altered after TBI because magnesium falls on the order of 50%. In addition to treating hypomagnesemia, administration of magnesium affords neuroprotection. Magnesium is an *N*-methyl-D-aspartate (NMDA) antagonist that suppresses excitotoxic mechanisms. Excitatory amino acids such as glutamate and aspartate are released after traumatic injury, which initiates a cascade of events leading to secondary injury. Glutamate-induced ionic depolarization leads to calcium influx and cell death. Magnesium works at the postsynaptic receptor to reduce the neurotoxic effect of glutamate. In animal models, TBI decreases intracellular free concentrations of magnesium. Magnesium crosses the blood–brain barrier. Repeated administration of magnesium attenuates brain edema and improves neurologic recovery. Although prophylactic magnesium administration has received some enthusiasm in the management of stroke, its clinical use in the treatment of head injury remains to be seen.

Cottrell JE. *Brain Protection in Neurosurgery. ASA Annual Refresher Course Lectures*. Park Ridge, IL: American Society of Anesthesiologists; 2004;145.

Fu ES, Tummala RP. Neuroprotection in brain and spinal cord trauma. *Curr Opin Anaesth*. 2005;18:181–187.

A.8. What role do gender and female sex hormones have in the pathophysiology of traumatic brain injury (TBI)?

Women account for approximately 20% to 30% of the head injury population. Laboratory evidence indicates that estrogen and progesterone mediate neuroprotection by decreasing lipid peroxidation and reducing production of inflammatory cytokines. Compared with women, increases in cerebrospinal fluid (CSF) levels of glutamate, lactate, and F_2-isoprostane (marker for lipid peroxidation) are observed in men after TBI. Nevertheless, there appears to be a paradox between the acute neuroprotective properties of female sex hormones and actual recovery for women as functional outcome has been worse for women. It has been suggested that female sex hormones may be detrimental to neuroplasticity and recovery. In addition to gender differences, the effect of hormonal status in female patients in the pathophysiology of head injury remains unclear. Consequently, gender selection and the relation of hormonal status at time of injury become important in the design of clinical trials involving therapeutic interventions in brain trauma patients. ProTECT, a National Institutes of Health–funded, randomized, double-blind phase III clinical trial, is underway to evaluate approximately 1140 patients over a 3- to 6-year period using the hormone progesterone to treat TBI at 17 medical centers across the United States.

Fu ES, Tummala RP. Neuroprotection in brain and spinal cord trauma. *Curr Opin Anesth.* 2005;18:181–187.

Wagner AK, Fabio A, Puccio AM, et al. Gender associations with cerebrospinal fluid glutamate and lactate/pyruvate levels after severe traumatic brain injury. *Crit Care Med.* 2005;33:407–413.

A.9. What is the role of decompressive craniectomy as a treatment option for intracranial pressure (ICP) control after head injury?

The objective of a decompressive craniectomy is to avoid or treat increases in intracranial pressure because of brain edema, because high ICP is the most frequent cause of death and disability from head injury. Usually, the first line of treatment for high ICP is moderate hypocapnia, mannitol, sedation, and normothermia. When these measures fail, more aggressive approaches such as decompressive craniectomies are employed to allow the brain to expand and prevent brain herniation. Nevertheless, the benefits of decompressive craniectomy has not been proven in a randomized controlled fashion. Therefore, routine use of this therapy cannot be recommended. At this juncture, many clinicians feel that this procedure should be considered only in clinical situation in which maximal medical therapy failed to control ICP.

Aarabi R, Hesdorffer DC, Simard JM, et al. Comparative study of decompressive craniectomy after mass lesion evacuation in severe head injury. *Neurosurgery.* 2009;64:927–940.

Paci GM, Sise MJ, Sise B, et al. Comparative study of decompressive craniectomy after mass lesion evacuation in severe head injury. *J Trauma.* 2009;67:531–536.

Sahuquillo J. Decompressive craniectomy for the treatment of refractory high intracranial pressure in traumatic brain injury. *Cochrane Database Syst Rev.* 2006;1:CD003983.

A.10. Do genetic factors play a role in the outcome after head injury?

An association exists between poorer outcomes after head injury in patients with the apolipoprotein E4 allele (APOE ε4). Two other isoforms, APOE 2 and APOE ε2, are other common isoforms to apolipoprotein E that have a different neurobiolgic function compared with that of APOE ε4, which appears to be less neuroprotective. In fact, APOE

ε4 is also associated with the risk of developing late-onset Alzheimer disease. In addition to apolipoproteins, interleukin (IL) proteins such as IL-1 have been implicated in neurodegeneration following ischemic insults and it is postulated that genetic polymorphisms in IL-1 may affect outcome after head injury. By understanding genetic polymorphisms in relation to head injury, targeted therapeutic approaches could be used on selected patients. One future drug on the horizon is bapineuzumab, which is used to treat Alzheimer disease in patients with a specific apolipoprotein E allele. Various authors have suggested that anti-inflammatory agents that block the cytokine and IL cascade could be used in patients with a certain IL-1 polymorphism.

ArizaM, Pueyo R, Matarin MM, et al. Influence of APOE polymorphism on cognitive and behavioral outcome in moderate and severe traumatic brain injury. *J Neurol Neurosurg Psychiatry*. 2006;77:1191–1193.

Dardiotis E, Fountas KN, Dardioti M, et al. Genetic association studies in patients with traumatic brain injury. *Neurosurg Focus*. 2010;28:1–12.

Diaz-Arrasti R, Baxter V. Genetic factors in outcome after traumatic brain injury: what the Human Genome Project can teach us about brain trauma. *J Head Trauma Rehabil*. 2006;21:361–374.

B. Preoperative Evaluation and Preparation

B.1. What is the GCS? What is the significance of a GCS of 8 in this patient?

The GCS is the most widely used method to assess neurologic status and severity of brain dysfunction following head trauma. The GCS has been shown to have a significant correlation with outcome following severe head injury both as a sum score and the motor component. The scale, which ranges from 3 to 15 points, is based on evaluating the best motor response, the best verbal response, and the eye opening (Table 19.1).

Table 19.1 Glasgow Coma Scale

Eye opening:	None	1
	To pain	2
	To verbal command	3
	Spontaneous	4
Best verbal response:	No verbal response	1
	Incomprehensible sounds	2
	Inappropriate words	3
	Disoriented, conversing	4
	Oriented, conversing	5
Best motor response:	No response (flaccid)	1
	Extension (decerebrate)	2
	Abnormal flexion (decorticate)	3
	Flexion/withdrawal	4
	Localizes to pain	5
	Obeys verbal commands	6

Of the patients who initially survive TBI, 80% have minor injury (GCS 13 to 15), 10% have moderate injury (GCS 9 to 12), and 10% have severe injury (GCS ≥8). Serial determination of GCS is essential to monitor the patient's condition because GCS can change in a rapid or delayed manner. Decreases in the GCS of three or more points are indicative of catastrophic neurologic deterioration.

Glasgow Coma Scale. *J Neurotrauma*. 2000;17:563–571.

Schmidek HH, ed. *Operative Neurosurgical Techniques*. 4th ed. Philadelphia: WB Saunders; 2000:83–85.

B.2. In addition to the GCS, what other assessments can be done to evaluate neurologic function?

The GCS assesses spontaneous activity. Further neurologic evaluation includes pupillary examination, checking for brainstem reflexes in unconscious patients, and looking for lateralizing signs. Fixed bilateral enlarged pupils may signify an ominous prognosis, whereas unilateral pupillary enlargement occurs in the presence of an expanding hematoma or isolated ocular trauma. Deeply comatose patients lacking spontaneous eye opening should have evaluation of the brainstem reflexes. The oculocephalic reflex, or doll's eye maneuver, is elicited by rotating the head horizontally to one side. In the intact brainstem, the eyes deviate conjugately to the other side. This maneuver should be performed only when the cervical spine has been cleared. If the doll's eye response is abnormal, testing of the oculovestibular reflex (cold caloric test) is another method to evaluate brainstem function. The cold caloric test entails irrigation of the external auditory canal with ice water. In the intact brainstem, the eyes should deviate to the side of cold stimulation. Abnormal oculocephalic and oculovestibular reflexes signify severe brainstem dysfunction extending to the pons. However, other causes for abnormal responses need to be ruled out, which include drugs (e.g., phenytoin), nerve injuries (e.g., oculomotor, abducens, vestibular), and labyrinthine disease. Additional lateralizing signs include asymmetric posturing, hemiparesis, and facial weakness. The presence of these findings could indicate the possibility of a mass lesion.

Cottrell JE, Smith DS, eds. *Anesthesia and Neurosurgery*. 5th ed. St. Louis: Mosby; 2010:669–670.

Cucchiara RF, Black S, Michenfelder JD, eds. *Clinical Neuroanesthesia*. 2nd ed. New York: Churchill Livingstone; 1998:241–242.

B.3. What is the role of CT scanning in the initial evaluation of the patient with head injury? What management options can be done in patients whose neurologic condition is deteriorating before obtaining a CT scan?

Several checklist-based criteria for brain CT exist: the Canadian CT Head Rule and the New Orleans Criteria. These criteria have proven to be efficacious but, in general, if there has been a loss of consciousness or if the GCS is less than 15, a head CT scan should be obtained. Evidence of an intracranial hematoma that causes compression of the ventricles or a midline shift of greater than 5 mm is an indication for surgical intervention. Conversely, absence of a mass lesion or compression of the ventricles is an indication for conservative management. In a patient whose neurologic condition is deteriorating, securing the airway, hyperventilation, administration of hyperosmolar therapy, and sedation (with or without muscle relaxants) may provide sufficient time to obtain a preoperative CT scan. In rare circumstances, the surgeon may need

to initiate emergency surgical exploration of an expanding intracranial hematoma without CT scanning. Even more rare, in acute situations, urgent partial surgical decompression through a burr hole close to the fracture may be required.

Cottrell JE, Smith DS, eds. *Anesthesia and Neurosurgery*. 5th ed. St. Louis: Mosby; 2010: 665–668.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. New York: Churchill Livingstone; 2010:2152.

Prough DS. *Update on CNS Injury: Fluid and Metabolic Management of the Neurosurgical Patient. ASA Annual Refresher Course Lectures*. Park Ridge, IL: American Society of Anesthesiologists; 2008:331.

Schmidek HH, ed. *Operative Neurosurgical Techniques*. 4th ed. Philadelphia: WB Saunders; 2000:83–85.

B.4. What is the role of ICP monitoring in the management of head injury?

Life-threatening emergencies such as impending herniation or hemorrhagic wounds in the abdomen or thorax require rapid surgical intervention. Definitive surgery for non–life-threatening cranial injuries should be delayed until the patient is hemodynamically stable to minimize hypotension, hypovolemia, and cerebral hypoxemia. If the patient is not emergently taken to the operating room, ICP monitoring becomes helpful in optimizing blood pressure management because CPP can be calculated by measuring mean arterial pressure (MAP) and ICP. Patients with head trauma often sustain other injuries requiring nonneurologic surgery. The decision to have an ICP monitor placed before nonneurologic surgery includes neurologic status in conjunction with CT findings, the nature and duration of the surgical procedure, and surgical procedures requiring occlusion of the aorta.

Although no prospective, randomized clinical trials have been conducted to establish the clinical efficacy of ICP monitoring, it has become widely used for the diagnosis and management of intracranial hypertension. ICP monitoring helps in the early detection of expanding hematomas and can be useful in reducing ICP by CSF drainage.

ICP monitoring is appropriate in this case because this patient has severe brain injury and an abnormal CT scan. In patients with severe head injury but a normal CT scan, ICP monitoring is indicated when systolic blood pressure is less than 90 mm Hg and there is motor posturing. ICP monitoring is rarely indicated in patients with mild to moderate injury.

Marion DW, Spiegel TP. Changes in the management of severe traumatic brain injury. 1991–1997. *Crit Care Med.* 2000;28:16–18.

Marshall LF. Head Injury: recent past, present and future. *Neurosurgery.* 2000;47:546–561.

Prough DS. Perioperative *Management of Traumatic Brain Injury. ASA Annual Refresher Course Lectures*. Park Ridge, IL: American Society of Anesthesiologists; 2004:221.

Schmidek HH, ed. *Operative Neurosurgical Techniques*. 4th ed. Philadelphia: WB Saunders; 2000:83–85.

B.5. How can you clear this patient's cervical spine?

Patients presenting to trauma units following closed head injury may have a concomitant cervical spine fracture. Adequate cervical spine radiographs, especially in the uncooperative patient, are very difficult to obtain following many traumas. Furthermore, injuries in the atlanto-occipital region are especially difficult to identify radiographically, and up to 26% of lateral radiographs failed to show fractures.

Even in the face of normal radiographic studies, patients may still have significant ligamentous injuries with cervical instability necessitating particular care during airway management. Typically, patients are examined carefully, their cervical spine is palpated, and tenderness or weakness is identified. In the uncooperative or unconscious patient, the cervical spine should be considered not cleared, even in light of normal radiographs. On the other hand, if the cervical spine is cleared radiographically, the mental status is normal, and the patient is asymptomatic, then the examination can be considered cleared.

Brooks RA, Willett KM. Evaluation of the Oxford protocol for total spinal clearance in the unconscious trauma patient. *J Trauma.* 2001;50:862–867.

Miller RD, ed. *Miller's Anesthesia*, 7th ed. New York: Churchill Livingstone; 2010.

Stiell IG, Wells GA, Clement C, et al. The role of clinical assessment in the evaluation of patients with potential cervical spine injury. *Acad Emerg Med.* 2001;8:457.

Todd MM. *Cervical Spine Motion: Cervical Spine Injury and the Unstable Neck. ASA Annual Refresher Course Lectures.* Park Ridge, IL: American Society of Anesthesiologists; 2008:506.

B.6. What are the benefits of early endotracheal intubation in this patient?

Endotracheal intubation not only provides a secure airway in a patient with an altered ability to protect the airway, but also allows for the ability to provide optimum oxygenation and hyperventilation of the patient, thereby providing a rapid tool for lowering ICP if necessary. Also, patients with facial trauma can often have progressive swelling and anatomic distortion, making subsequent intubation attempts more difficult.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. New York: Churchill Livingstone; 2010.

Bendo AA. *Update on CNS Injury: Adult Head Injury Management—Are Guidelines Improving Outcome. ASA Annual Refresher Course Lectures.* Park Ridge, IL: American Society of Anesthesiologists; 2008:331.

B.7. What is your plan for airway management in this patient? How would it change if the patient were combative? How would it change if the patient had facial fractures with significant swelling of the head and neck?

Patients with a GCS less than 8 often require intubation and controlled ventilation to lower the ICP and protect the airway. Direct laryngoscopy following induction and muscle relaxation should be accompanied by in-line stabilization by an assistant, with many authors recommending leaving the posterior portion of the rigid collar in place, so that it can act as a stabilizer to prevent further movement. Earlier recommendations for in-line traction are no longer popular because of concerns for spinal cord damage in patients with gross instability. Emergency airway equipment should always be available in case of the inability to intubate with direct laryngoscopy. Another option is awake fiberoptic intubation, but a compliant patient is a necessity, because thrashing and fighting can cause more harm to the unstable spine than laryngoscopy itself. A combative patient would make one lean more toward rapid sequence induction and intubation with in-line stabilization, whereas a patient with facial fractures and facial swelling would lead one to fiberoptic intubation. Midface and basilar skull fractures should preclude attempts at nasal intubation because of concerns for entering the cranial vault inadvertently. Blood in the airway can complicate fiberoptic

intubation in these patients, and alternative intubation devices and plans should be readily available. In any event, the goals of preoxygenation and securing an airway with minimum cervical spine motion should be observed, while being cognizant of the risk for regurgitation and aspiration in a patient with a full stomach.

Miller RD, ed. *Miller's Anesthesia.* 7th ed. New York: Churchill Livingstone; 2010.

Todd MM. *Cervical Spine Motion: Cervical Spine Injury and the Unstable Neck. ASA Annual Refresher Course Lectures.* Park Ridge, IL: American Society of Anesthesiologists; 2008:506.

B.8. What are the effects of succinylcholine on ICP? What is the significance of the effect, if any?

Succinylcholine has been shown in animal and human studies to increase ICP through increased muscle spindle activation with depolarization. The effect can be avoided by using a defasciculating dose of a nondepolarizing drug before succinylcholine administration. It is important to remember that the elevation in ICP from succinylcholine will be much less than the elevation during intubation attempts in awake struggling patients.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. New York: Churchill Livingstone; 2010.

B.9. What coagulation abnormalities are present after TBI? What treatment modalities can be used to provide hemostasis and reduce intracranial hematoma expansion?

Disseminated intravascular coagulation (DIC) is a consequence of TBI, presumably related to release of tissue thromboplastins. One explanation for secondary brain injury after intracranial bleeding is ischemia secondary to cerebral herniation, increased ICP, and direct blood vessel occlusion by the hematoma. An alternative explanation is intravascular microthrombosis secondary to DIC.

In an aging population, the number of individuals taking warfarin for the prevention of thromboembolic complications of atrial fibrillation, cardiac valve replacement, deep venous thrombosis, and thrombophilic states increases. These individuals are at increased risk for intracranial hemorrhage from trauma or spontaneous causes, and their management has a poorer outcome and necessitates urgent reversal of anticoagulation for rapid surgical intervention. Traditionally, administration of fresh frozen plasma and clotting factors has been used in correcting coagulation abnormalities after head injury. Early hemostatic therapy for acute hemorrhage has been proposed to reduce the growth of hematoma expansion. Recombinant activated factor VIIa has been administered to promote hemostasis in patients with acute intracerebral hemorrhage. There are no definitive values regarding the international normalized ratio (INR) threshold beyond which surgery cannot safely be performed. A high mortality rate has been reported in the postoperative period in patients with preoperative INR values greater than 1.25; an INR of 1.2 to 1.5 is considered to be sufficient for neurosurgical hemostasis. Other investigators have suggested an INR of 1.3 to be the goal of preoperative warfarin (Coumadin) reversal.

Recombinant activated factor VIIa acts in a tissue factor–dependent manner, binding with high affinity to the surface of activated platelets and enhancing thrombin formation after direct activation of factors IX and X on the surface of the activated platelets. Its efficacy has been evaluated in many areas of medicine because recombinant activated factor VIIa significantly slowed progression of hemorrhage and reduced the morbidity and mortality after spontaneous intracerebral hemorrhage. Algorithms

have been developed to determine the use of recombinant factor VIIa in coagulopathy intracranial hemorrhage states based on the answer to two principal questions: (1) What is the type of bleeding and what is the risk for expansion of the hematoma? and (2) How urgent is the indicated surgery (timing)? Studies have verified that in regard to outcomes, surgical intervention early from admission is recommended for epidural hemorrhage or subdural hemorrhage with prominent clinical impairment or progressive deterioration. If not deteriorating rapidly, patients can be operated on within 24 hours.

Bartal C, Yitzhak A. The role of thromboelstometry and recombinant factor VIIa in trauma. *Curr Opin Anaesthesiol.* 2009;22:281–288.

Boulis NM, Bobek MP, Schmaier A, et al. Use of factor IX complex in warfarin-related intracranial hemorrhage. *Neurosurgery.* 1999;45:1113–1118.

Mathiesen T, Benediktsdottir K, Johnsson H, et al. Intracranial traumatic and non-traumatic haemorrhagic complications of warfarin treatment. *Acta Neurol Scand.* 1995;91:208–214.

Mayer SA. Ultra-early hemostatic therapy for primary intracerebral hemorrhage: a review. *Can J Neurol Sci.* 2005;2(suppl):S31–S37.

Mayer SA, Brun NC, Begtrup K, et al. Recombinant activated factor VII for acute intracerebral hemorrhage. *N Engl J Med.* 2005;352:777–785.

Stein DM, Dutton RP, Kramer ME, et al. Recombinant factor VIIa: decreasing time to intervention in coagulopathic patients with severe traumatic brain injury. *J Trauma.* 2008;64:620–628.

Stein S, Smith DH. Coagulopathy in traumatic brain injury. *Neurocrit Care.* 2004;1:479–488.

Yasuda CL, Morita ME, Nishimori FY, et al. [Chronic subdural hematoma: study of 161 patients and the relationship with coagulation abnormalities]. *Arq Neuropsiquiart.* 2003;61:1011–1014.

C. Intraoperative Management

C.1. What is appropriate hemodynamic monitoring during CT scanning and during craniotomy for evacuation of a subdural hematoma?

It is axiomatic that hemodynamic monitoring should be commensurate with the anticipated changes in cardiovascular status during the planned procedure. Assuming there is no evidence of occult blood loss or major intrathoracic injury, the most aggressive monitoring during CT scanning should consist of direct arterial pressure assessment. This is based on the requirement for arterial blood gas analysis and the possible need to administer vasoactive drugs to control blood pressure. Conversely, if there is evidence of occult bleeding or a major thoracic injury, placement of a central venous pressure (CVP) or pulmonary arterial catheter may be required in guiding fluid management before CT scanning.

If no invasive monitors were placed during CT scanning, an arterial line is needed before craniotomy surgery. Placement of a CVP or pulmonary artery catheter in the operating room is helpful in managing blood pressure in conjunction with fluid administration. If cardiac contusion is a consideration, placement of a pulmonary artery catheter would be preferable over placement of a CVP catheter, because both cardiac output and right ventricular pressures can be measured. Cardiac contusion is most often associated with right ventricular dysfunction.

C.2. Should hyperventilation be used in this patient?

The theoretical advantages of hyperventilation are control of ICP and reversal of acidosis in brain tissue. Cerebral blood flow in head-injured tissue is low, and

vasoconstriction can result in ischemia. In areas of severe injury (e.g., subdural hematomas, diffuse contusions), there is local variability in perfusion as well as loss of autoregulation and carbon dioxide reactivity. A randomized, clinical trial has shown that hyperventilation is potentially deleterious, suggesting that prophylactic hyperventilation ($Paco_2$ <35 mm Hg) should be avoided. It has been suggested that the use of monitors such as jugular venous hemoglobin oxygen saturation monitoring and cerebral oximeters may help determine the effects of hyperventilation on cerebral oxygenation. Measures of cerebral metabolism may predict which patients benefit from hyperventilation.

Currently, it has been recommended that hyperventilation be used on a selective rather than routine basis. Hyperventilation may be necessary to lower ICP for brief periods in which there is acute neurologic deterioration or intracranial hypertension that is refractory to other treatment modalities such as mannitol and CSF drainage. If ICP monitoring is present in the operating room, hyperventilation could be used to lower ICP to less than 20 mm Hg. Other goals such as facilitating surgical access and minimizing surgical retraction are still important considerations in the intraoperative management of head injury.

Brain Trauma Foundation; American Association of Neurological Surgeons; Congress on Neurological Surgeons, et al. Guidelines for the management of severe traumatic brain injury. XIV. Hyperventilation. *J Neurotrauma*. 2007;24(suppl 1):S87–S90.

Marshall LF. Head injury: recent past, present and future. *Neurosurgery*. 2000;47:546–561.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. New York: Churchill Livingstone; 2010.

C.3. What are the implications of arterial hypertension in patients with head injury? How should blood pressure be managed?

Hypertension is a common feature of head injury in patients who do not have massive blood loss associated with their injuries. The etiology of hypertension appears to be catecholamine related. Some experts believe that cerebral perfusion is optimized when there is a high arterial pressure opposing the effects of elevated ICP. Others think that in the presence of a disrupted blood–brain barrier, arterial hypertension contributes to extravasation of edema fluid and aggravation of brain swelling.

Although some experts advocate maintaining CPP above 60 mm Hg, proponents of high CPP recommend maintaining CPP greater than 70 mm Hg with the use of volume expansion and vasoactive drugs. Several clinical studies have suggested improved outcomes when systemic arterial pressure is raised to keep CPP at 70 to 90 mm Hg, but they were not controlled, blinded, or randomized. Other studies have questioned the necessity of vasopressors to maintain cerebral perfusion above 70 mm Hg and the role of CPP as a determinant of cerebral blood flow. The consensus at this time is to maintain arterial pressure at normal to slightly elevated levels. Above all, arterial hypotension is to be avoided, because it profoundly increases neuronal damage in the presence of elevated ICP.

Brain Trauma Foundation; American Association of Neurological Surgeons; Congress on Neurological Surgeons, et al. Guidelines for the management of severe traumatic brain injury. I. Blood pressure and oxygenation. *J Neurotrauma*. 2007;24(suppl 1): S7–S13.

Marshall LF. Head injury: recent past, present and future. *Neurosurgery*. 2000;47:546–561.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. New York: Churchill Livingstone; 2010.

C.4. What should be done about intravenous fluid replacement? Should corticosteroids be given empirically?

Often, many head-injured patients sustain multiple injuries that require aggressive resuscitation with crystalloids, plasma expanders, and blood. Once the patient arrives to the operating room, packed red blood cells should be administered to maintain normal CVP along with crystalloid or colloid solutions in quantities sufficient to replace blood loss. The problem with aggressive resuscitation is that excessive crystalloid administration may exacerbate brain edema.

Rapid formation of brain edema is a common reaction associated with most neuropathologic processes, including intracranial hematomas. Although crystalloid administration decreases colloid oncotic pressure, the reduction of colloid oncotic pressure does not cause edema in normal or injured brain tissue. It is the administration of free water and the decrease in osmolality that appear to be important in edema formation. In experimental studies, D_5W solutions increase edema, increase blood glucose, and worsen neurologic outcome. Isotonic solutions such as isolyte and 0.9% saline have no adverse effect on edema formation, blood glucose, and neurologic outcome. The worsening of neurologic outcome with D_5W has been attributed to edema formation rather than hyperglycemia. Hypotonic solutions (D_5W, 1/2 normal saline) should *not* be used in the patient with TBI. The ideal volume state for a patient with brain injury is hypertonic and euvolemic, which can be achieved with normal saline or hypertonic solutions.

Corticosteroids have been shown to be effective in reducing cortical vasogenic edema associated with brain tumors and abscesses, but level I data, in the Corticosteroid Randomization After Significant Head Injury (CRASH) study, determined that they lack efficacy in head trauma. Corticosteroids failed to demonstrate any benefit and are occasionally associated with iatrogenic complications such as sepsis. Glucocorticoids do not lower ICP, and routine use is not recommended for head injury. Moreover, their potential for raising plasma glucose make their use less desirable in the setting of TBI.

Marshall LF. Head injury: recent past, present and future. *Neurosurgery*. 2000;47:546–561.

Prough DS. *Update on CNS Injury: Fluid and Metabolic Management of the Neurosurgical Patient. ASA Annual Refresher Course Lectures*. Park Ridge, IL: American Society of Anesthesiologist; 2008:331.

Talmor D, Shapira Y, Artru AA, et al. 0.45% saline and 5% dextrose in water, but not 0.9% or 5% dextrose in 0.9% saline, worsen brain edema two hours after closed head trauma in rats. *Anesth Analg*. 1998;86:1225–1229.

C.5. Should hypertonic saline be administered to this patient? How is hypertonic saline administered?

The rationale for hyperosmolar therapy is to decrease cerebral edema by creating an osmolar gradient between the intravascular space and cerebral tissue. Water moves from the cells and interstitial spaces into the capillaries, to decrease cerebral water content and ICP. Hypertonic saline and mannitol are the modalities for hyperosmolar therapy. Hypertonic saline has been shown to decrease ICP even when other conventional measures such as barbiturates and mannitol have been exhausted. Hypertonic saline is a volume expander in the systemic circulation and does not impair renal function as seen with mannitol administration. Often, with hypertonic saline administration, the goal is to maintain normovolemia with the help of CVP or pulmonary arterial catheter monitoring.

Typically, a 3% saline solution is administered at a rate of 75 to 150 mL per hour; whereas a bolus of 250 mL may be given for aggressive therapy. Of further note, the use of 7.5% hypertonic saline has been reported. Preliminary evidence supports the use of hypertonic saline in reducing ICP, suggesting that controlled clinical trials should be performed to determine if hypertonic saline improves outcome. Currently, the human data are still inconclusive to recommend the use of hypertonic saline as a

standard of management. In one study, patients receiving 2 mL per kg of 7.5% saline had better control of ICP than patients receiving mannitol but no changes in mortality or neurologic outcome were observed. In another study involving the prehospital administration of hypertonic saline for resuscitation in patients with hypotension and TBI, ICP control was better in the patients receiving hypertonic saline, but again no differences in outcome were demonstrated.

Cooper DJ, Myles PS, McDermott FT, et al. Prehospital hypertonic saline resuscitation of patients with hypotension and severe traumatic brain injury: a randomized controlled trial. *JAMA*. 2004;291:1350–1357.

Horn P, Munch E, Vajkoczy P, et al. Hypertonic saline solution for control of elevated intracranial pressure in patients with exhausted response to mannitol and barbiturates. *Neurol Res*. 1999;21:758–764.

Qureshi AI, Suarez JI. Use of hypertonic saline solutions in treatment of cerebral edema and intracranial hypertension. *Crit Care Med*. 2000;28:3301–3313.

Qureshi AI, Suarez JI, Bhardwaj A, et al. Use of hypertonic (3%) saline/acetate infusion in the treatment of cerebral edema: effect on intracranial pressure and lateral displacement of the brain. *Crit Care Med*. 1998;26:440–446.

Vialet R, Albanese J, Thomachot L. Isovolume hypertonic solutes (sodium chloride or mannitol) in the treatment of refractory posttraumatic intracranial hypertension: 2 mL/kg 7.5% saline is more effective that 2 mL/kg 20% mannitol. *Crit Care Med*. 2003;31:1683–1687.

C.6. The patient underwent a craniectomy for evacuation of a frontal intracerebral hematoma. Should some anesthetic agents be avoided in this situation? Which ones? What agents might be preferred in this situation?

The principles of anesthetic management for patients with rapidly expanding intracranial mass lesions are based on the idea of maximizing intracranial compliance by minimizing the volume within the intracranial compartment. This means that any maneuver that increases cerebral blood volume should be avoided. All intravenous induction agents (e.g., thiopental, etomidate, and propofol) except for ketamine are known for their vasoconstrictive effects and are reasonable choices provided that the hemodynamic stability is maintained. Ketamine has been out of favor in the neurosurgical setting because early studies showed that it increases cerebral metabolic rate, cerebral blood flow, and ICP. A more recent study showed that in ventilated patients receiving propofol sedation, ketamine actually decreased ICP and did not adversely alter cerebral hemodynamics. These authors surmised that when ketamine is added to a background anesthetic, the central nervous excitation effects of ketamine are blunted and it increases the depth of anesthesia. Because ketamine is an NMDA antagonist, with possible neuroprotective effects, it has been suggested that the use of ketamine in head injury warrants reevaluation.

All of the volatile inhalation agents and nitrous oxide have some cerebral vasodilatory effects. Caution must be exercised in using inhalation agents in patients with rapidly expanding intracranial mass lesions. When the surgical field is "tight," eliminating inhalation agents and going with a total intravenous anesthetic technique may be appropriate. For example, a propofol or thiopental infusion may render the patient sufficiently anesthetized for a craniotomy. Finally, concern exists that opioids may act as cerebral vasodilators and raise ICP. Several studies have shown that sufentanil increases ICP in patients with head injury possibly secondary to indirect cerebral vasodilatation caused by autoregulatory compensation when MAP decreases. Direct cerebral vasodilatation has been implicated in the increase in ICP seen after morphine and fentanyl administration.

Albanèse J, Arnaud S, Rey M, et al. Ketamine decreases intracranial pressure and electroencephalographic activity in traumatic brain injury patients during propofol sedation. *Anesthesiology*. 1997;87:1328–1334.

de Nadal M, Munar F, Poca MA, et al. Cerebral hemodynamic effects of morphine and fentanyl in patients with severe head injury: absence of correlation to cerebral autoregulation. *Anesthesiology*. 2000;92:11–19.

C.7. Should hypothermia be employed in this patient?

In experimental models, hypothermia has been shown to decrease the amount of edema and necrosis volume after cerebral damage. A temperature of 33° C (91.4° F) has been considered to be the safe limit for patients with head injury. Several clinical trials, involving less than 100 patients, have shown that inducing moderate (32° C to 33° C [89.6° F to 91.4° F]) or mild hypothermia (33° C to 35° C [91.4° F to 95° F]) in patients with severe head trauma (GCS less than 8), improves neurologic outcome. Nevertheless, a multicenter phase III head injury trial, involving almost 400 patients, showed that inducing hypothermia in patients who had already arrived to the hospital normothermic did not improve outcome. In general, enthusiasm for the application of hypothermia in neurosurgical patients has faded as another multicenter trial of hypothermia involving cerebral aneurysm patients also demonstrated negative findings in improving neurologic outcome. Despite negative findings from the most recent comprehensive trials on hypothermia, various researchers contend that the complete abandonment of hypothermia is premature and newer technologies that induce hypothermia (e.g., intravascular cooling) should be further investigated.

Clifton GL, Miller ER, Choi SC, et al. Lack of effect of induction of hypothermia after acute brain injury. *N Engl J Med*. 2001;344:556–563.

Jiang J, Yu M, Zhu C. Effect of long-term mild hypothermia therapy in patients with severe traumatic brain injury: 1-year follow-up review of 87 cases. *J Neurosurg*. 2000;93:718–719.

Marion DW, Penrod LE, Kelsey SF, et al. Treatment of traumatic brain injury with moderate hypothermia. *N Engl J Med*. 1997;336:540–546.

Sahuquillo J, Mena MP, Vilalta A, et al. Moderate hypothermia in the management of severe traumatic brain injury: a good idea proved ineffective? *Curr Pharm Des*. 2004;10:2193–2204.

Todd MM, Hindman BJ, Clarke WR, et al. Mild intraoperative hypothermia during surgery for intracranial aneurysm. *N Engl J Med*. 2005;352:135–145.

D. Postoperative Neurointensive Care Management

D.1. What are the postoperative ventilation considerations in this patient?

If the patient had normal consciousness preoperatively, early extubation would be preferable once it is confirmed that the patient is able to follow commands and move extremities. Efforts should be made to avoid bucking and coughing on the endotracheal tube and to treat hypertension that occurs on emergence. Intravenous lidocaine is a useful drug to smooth the coughing associated with emergence. Short-acting opiates, particularly remifentanil, can provide a smooth emergence in patients that are hemodynamically stable, tolerating the endotracheal tube, and following commands. However, many patients with TBI undergoing emergency surgery remain intubated postoperatively because of the severity of the brain injury. In that case, blood pressure

control to prevent hypertension is needed to prevent further hemorrhage. In some patients, sedatives and muscle relaxants may be administered on transport to prevent changes in ICP associated with stimulation and agitation. In ventilated patients, the use of a cerebral oxygen monitor may be useful in optimizing brain oxygen delivery in relation to $Paco_2$.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. New York: Churchill Livingstone; 2010.

Prough DS. *Perioperative Management of Traumatic Brain Injury. ASA Annual Refresher Course Lectures*. Park Ridge, IL: American Society of Anesthesiologists, 2004:221.

D.2. What specific measures should be used to control the patient's ICP? What type of monitoring devices can be used to monitor ICP?

After removal of a mass occupying lesion, control of ICP is of paramount importance in the patient's recovery. Briefly, those patients whose ICP can be maintained below 20 to 25 mm Hg tend to have significantly better outcomes than do patients whose ICP remain elevated. It has become common practice, therefore, to monitor ICP in the postoperative period in these patients. This enables the intensivist to adjust treatment with hyperventilation, mannitol, CSF drainage, and head-up tilt to the desired ICP response. If these maneuvers fail, the next intervention is to maintain barbiturate coma to a level at which the electroencephalogram shows burst suppression. This is continued until it is no longer necessary to control intracranial hypertension. After weaning from barbiturate therapy, the patient can be weaned from diuretics and hyperventilation, as appropriate. As mentioned earlier, the use of hyperventilation in patients with head injury must be on a selective basis because hyperventilation has potentially deleterious effects on cerebral perfusion.

The classic intraventricular catheter or ventriculostomy was introduced by Lundberg in 1960 and has been the gold standard for ICP monitoring and CSF drainage. Placement of an intraventricular catheter has been associated with the potential for infection and brain parenchyma injury. Placement of a subarachnoid bolt used to be a less invasive modality but limitations included accuracy and stability. Subarachnoid bolts have been supplanted by a variety of implantable pressure transducer devices. Current ICP monitoring systems use a twist drill for bolt placement in the skull to allow a catheter to be rapidly placed in the parenchyma or subarachnoid space. Some systems allow CSF drainage in which a catheter containing a transducer at the tip is placed into the ventricles.

Brain Trauma Foundation; American Association of Neurological Surgeons; Congress on Neurological Surgeons, et al. Guidelines for the management of severe traumatic brain injury. VII. Intracranial pressure monitoring technology. *J Neurotrauma*. 2007;24(suppl 1):S45–S54.

Cucchiara RF, Black S, Michenfelder JD, eds. *Clinical Neuroanesthesia*. 2nd ed. New York: Churchill Livingstone; 1998:83–84.

Marshall LF. Head injury: recent past, present and future. *Neurosurgery*. 2000;47:546–561.

D.3. What is neurogenic pulmonary edema? Would you avoid positive end-expiratory pressure (PEEP) in a patient with increased ICP?

Neurogenic pulmonary edema is a commonly seen disorder following head injury or intracranial bleed. The mechanisms are unclear, but are thought to be due to a combination of increased pulmonary pressures resulting from massive catecholamine release with increased ICP (Cushing response) and altered pulmonary capillary permeability from as yet undescribed neurogenic factors. The onset can be immediate or

delayed, and treatment consists of supportive care as with other cases of pulmonary edema, including PEEP.

Positive pressure ventilation, PEEP, and increased ICP have been studied in animal and human models, and although there is a slight increase in ICP with higher levels of PEEP (10 to 12 cm H_20) in patients with normal ICP, patients with elevated ICP do not seem to demonstrate a clinically significant change in ICP with even high levels of PEEP. On the other hand, avoidance of PEEP, in such setting, may lead to hypoxemia that, in turn, can exacerbate cerebral ischemia.

McGuire G, Crossley D, Richards J, et al. Effects of varying levels of positive end-expiratory pressure on intracranial pressure and cerebral perfusion pressure. *Crit Care Med*. 1997;25:1059–1062.

Rosen P, ed. *Emergency Medicine: Concepts and Clinical Practice*. 4th ed. St. Louis: Mosby; 1998:436.

D.4. What is the role of antiseizure prophylaxis in the perioperative management of head trauma?

Seizures may cause secondary injury as a result of increases in ICP, changes in oxygen supply and demand, and increases in neurotransmitter release. Early posttraumatic seizures occur in the first week after injury, mostly within the first 24 hours. Late posttraumatic seizures occur after the first week. Often, early posttraumatic seizures occur within hours after injury, especially in patients with depressed or open skull fractures and hemorrhagic brain contusions. Short-term prophylactic administration of anticonvulsant drugs (e.g., phenytoin, carbamazepine) for early posttraumatic seizures is recommended. Recently, levetiracetam has gained popularity as monotherapy for the prevention of posttraumatic seizures. Levetiracetam has a favorable side effect profile compared with phenytoin and carbamazepine. Nevertheless, administration of anticonvulsant medicines has not been shown to prevent late posttraumatic seizures. Therefore, routine antiseizure prophylaxis is not recommended later than 1 week following head injury. Penetrating head injury may require longer posttraumatic seizure prophylaxis.

Marshall LF. Head injury: recent past, present and future. *Neurosurgery*. 2000;47:546–561.

Schmidek HH, ed. *Operative Neurosurgical Techniques*. 4th ed. Philadelphia: WB Saunders; 2000:54–56.

Szaflarski JP, Sangha KS, Linsell CJ, et al. Prospective, randomized, single-blinded comparative trial of intravenous levertiracetam versus phenytoin for seizure prophylaxis. *Neurocrit Care*. 2010;12:165–172.

D.5. How can cerebral oxygenation monitoring be used in the clinical management of TBI?

An indwelling parenchymal device that measures local oxygenation can be used to gain information regarding tissue oxygenation in real time at the bedside. In a severely injured brain, autoregulatory mechanisms fail. As a result, various areas of the brain will be ischemic. Use of an oxygen sensor allows for more precise management to optimize oxygen delivery and eliminate progression of ischemia. A cerebral oxygen monitor is placed either intraoperatively or at the bedside, much like a ventriculostomy. Many studies have shown it to be equally as useful as a jugular bulb catheter. The device can either be placed in an ischemic penumbra of a lesion or in an uninjured area of the brain. In the first case, the monitor will yield information that can be used to prevent further ischemia and cell death. In the second case, the device is used as a global indicator of cerebral oxygenation and may be useful in guiding ventilatory management.

Cerebral oxygenation monitoring also offers the ability to measure parenchymal temperatures simultaneous to oxygen content. This is of critical importance when using hypothermia or maintaining normothermia. By definition, brain oxygen tension or partial pressure (P_bO_2) is not adequate if it drops below 20 mm Hg. In recent studies, values less than 20 mm Hg for short intervals have correlated with worse neurologic outcome. A value greater than 30 mm Hg is optimal. Currently, there are several devices on the market that measure oxygen content.

Jaeger M, Soehle M, Meixensberger J. Brain tissue oxygen ($PtiO_2$): a clinical comparison of two monitoring devices. *Acta Neurochir (Wien).* 2005;95(suppl):79–81.

Jaeger M, Soehle M, Schuhmann MU, et al. Correlation of continuously monitored regional cerebral blood flow and brain tissue oxygen. *Acta Neurochir (Wien).* 2005;147:51–56.

Stiefel MF, Heuer GG, Smith MJ, et al. Cerebral oxygenation following decompressive hemicraniectomy for the treatment of refractory intracranial hypertension. *J Neurosurg.* 2004;101:241–247.

D.6. What methods can be used in the neurointensive care unit to prevent hyperthermia?

Fever continues to be a problem in critically ill neurosurgical patients. One retrospective study noted that more than 50% of patients with closed head injury had one febrile episode in the neurointensive care unit. Fever and hyperthermia accentuate excitotoxic release of neurotransmitters, increase production of free radicals, and accelerate cytoskeletal protein degradation. Although the enthusiasm to induce perioperative hypothermia for neuroprotection has waned, interventions are needed to cool patients to prevent hyperthermia.

Acetaminophen remains the first line of treatment for fever. Conventional water-circulating cooling blankets have been considered to be ineffective because of poor surface contact with the skin. A newer external cooling device has been developed that utilizes self-adhesive, hydrogel-coated pads that circulate temperature-controlled water under negative pressure. Intravascular central venous catheters have been developed for both cooling and rewarming. These catheters contain special built-in balloons through which cooled or warmed saline is circulated in a closed loop design. The patient's temperature is continuously compared with a user-defined target temperature, and the controller system is equipped with a safety system that sounds an alarm when the temperature is above or below programmed levels or when there is a system malfunction. Figure 19.3 shows a comparison of brain and rectal temperatures after intravascular cooling through a femoral catheter. Intracranial temperature measurements were obtained through an indwelling cerebral oxygen catheter placed into the brain parenchyma of the left frontal region.

In view of the recent advances in technologies to lower temperature, experts contend that it is premature to completely abandon the use of hypothermia. Future avenues of research include evaluating the impact of fever and hyperthermia on neurologic outcome, treating refractory elevations in ICP with hypothermia, and exploring methods for intraventricular or lumbar irrigation for rapid brain cooling.

Kilpatrick MM, Lowry DW, Firlik AD, et al. Hyperthermia in the neurosurgical intensive care unit. *Neurosurgery.* 2000;47:850–856.

Mayer SA, Kowalski RG, Presciutti M, et al. Clinical trial of a novel surface cooling system for fever control in neurocritical care patients. *Crit Care Med.* 2004;32:2508–2515.

Sahuquillo J, Mena MP, Vilalta A, et al. Moderate hypothermia in the management of severe traumatic brain injury: a good idea proved ineffective? *Curr Pharm Des.* 2004;10:2193–2204.

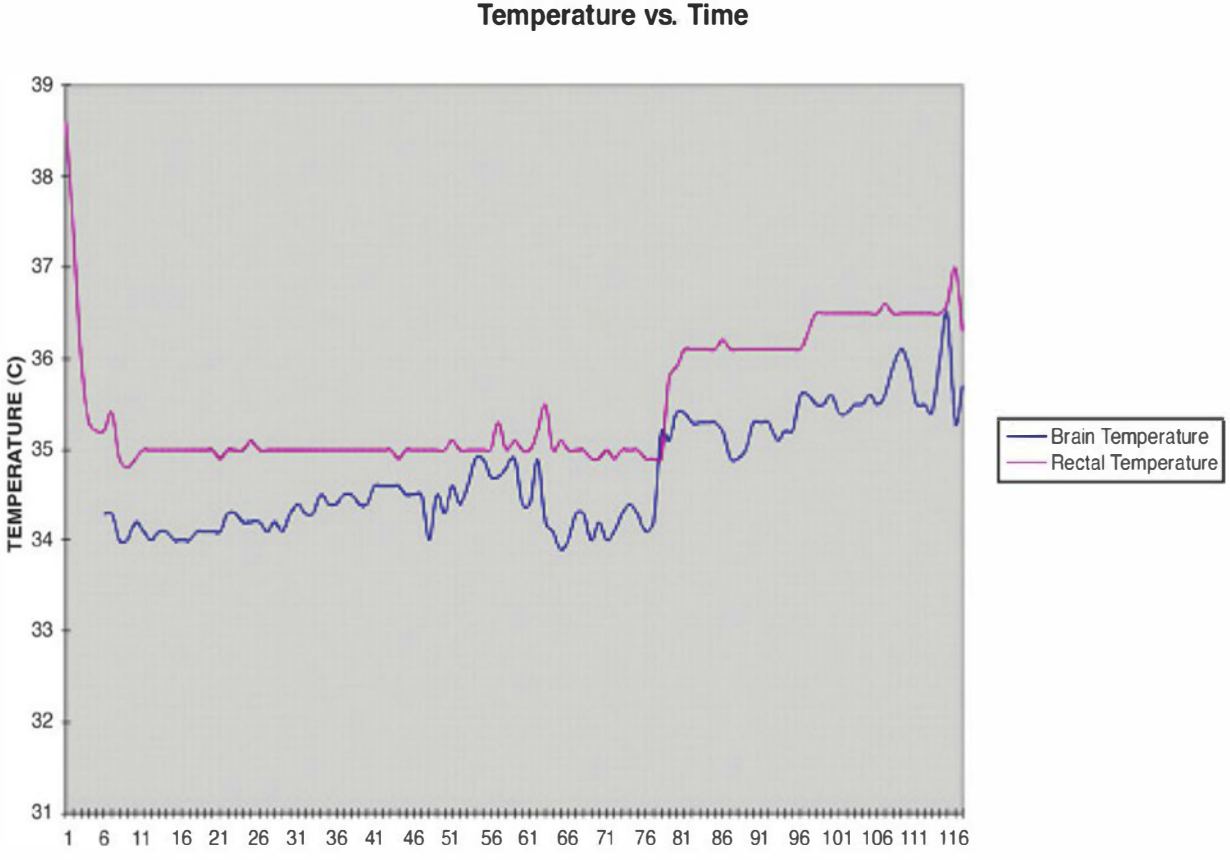

Figure 19.3 Comparison of brain and rectal temperatures following intravascular cooling. Intracranial temperatures were measured with a brain tissue oxygen catheter placed into the parenchyma of the left frontal region.

CHAPTER 20

Cerebral Aneurysm

Patricia Fogarty Mack

A 43-YEAR-OLD WOMAN presented to the emergency room 2 days ago, complaining of severe headache, nausea, and vomiting, followed by a witnessed 3-minute loss of consciousness. On regaining consciousness, the patient was noted by her family to be confused. A computed tomography (CT) scan showed subarachnoid bleeding. You are called to the angiography suite because four-vessel angiography has revealed an 18-mm basilar-tip aneurysm and a 10-mm right middle cerebral artery aneurysm. The interventional neuroradiologist wishes to coil the basilar tip aneurysm but believes the middle cerebral artery aneurysm will require craniotomy and clipping. At present, she was oriented only to person. She had no previous medical history; however, she had smoked one pack of cigarettes per day for the last 20 years. Blood pressure was 130/80 mm Hg, pulse 90 beats per minute, and respiration 18 breaths per minute. She had no focal neurologic deficits. Laboratory examination revealed normal electrolytes and complete blood count. Electrocardiogram demonstrated normal sinus rhythm with flipped T waves throughout the precordium.

A. Medical Disease and Differential Diagnosis

1. What are the incidence, prevalence, and causes of subarachnoid hemorrhage (SAH) and what are the risk factors associated with rupture of intracranial aneurysms?
2. What are common sizes and locations of intracranial aneurysms?
3. What is the pathophysiology of aneurysmal rupture and SAH?
4. What are symptoms and signs of SAH?
5. How does one assess the severity of SAH?
6. What are the cardiovascular effects of SAH?
7. How is the diagnosis of SAH made?
8. What is the risk for rebleeding for a patient with SAH?

B. Preoperative Evaluation and Preparation

1. What are some concerns in going to the interventional neuroradiology suite in the midst of an angiogram to follow immediately with coiling of an aneurysm?
2. What type of anesthesia is required for coiling of an aneurysm?
3. Would you proceed with induction of general anesthesia under these circumstances?
4. What types of emergencies can occur during coiling of an aneurysm and how should they be managed?
5. A craniotomy is planned for the following day to clip the middle cerebral artery aneurysm. Should surgery be postponed because of the patient's elevated creatinine phosphokinase (CPK) myocardial-bound (MB) fractions?
6. Would you premedicate this patient before craniotomy?

C. Intraoperative Management

1. What are the goals of the induction and maintenance of anesthesia for this patient?
2. Is placement of an arterial line necessary for induction of anesthesia in this patient in the interventional neuroradiology suite?
3. How would you assess fluid status in this patient?
4. Would monitoring central venous pressure (CVP) be useful in this patient for craniotomy for clipping?
5. What other forms of monitoring would you consider?
6. What are your particular concerns during induction of anesthesia in this patient?
7. How would you accomplish a smooth and safe induction and intubation of this patient?
8. Would you perform a rapid-sequence induction and intubation on this patient?
9. What are the effects of hypoxemia and hypercapnia, such as would be seen with loss of the airway on induction, on cerebral blood flow (CBF)?
10. What is optimal fluid management for aneurysm clipping? Would you use a dextrose-containing solution?
11. After the bone plate was removed and as the dura was being opened, the surgeon complained that the brain was "tight." What could you do to achieve better brain relaxation and facilitate surgical exposure?
12. How might transmural pressure be decreased to allow for aneurysm clip placement?
13. What is the purpose of controlled hypotension and how is it achieved?
14. What are some of the potential drawbacks of controlled hypotension?
15. What methods of cerebral protection might you employ during this operation?
16. Would you induce mild hypothermia as a means of cerebral protection?
17. What are the indications for deep hypothermic circulatory arrest?
18. What steps should be taken in the case of intraoperative rupture of an intracranial aneurysm?
19. How would you plan the emergence from an anesthetic for aneurysm clipping?

D. Postoperative Management

1. Would you extubate the patient postoperatively?
2. What would be the differential diagnosis if the patient did not return to her preoperative neurologic condition?

3. On postoperative day 2, the patient became disoriented and developed hemiplegia. A CT scan was obtained, which shows no new intracranial bleeding. What other diagnostic studies should be performed?
4. What is cerebral vasospasm and what causes it?
5. What are pathophysiologic changes seen in cerebral vasospasm?
6. How is the diagnosis of cerebral vasospasm made?
7. What steps can be taken to prevent cerebral vasospasm?
8. What treatments can be undertaken once a diagnosis of cerebral vasospasm is made?
9. What are other neurologic complications following SAH and aneurysm clipping?
10. What other organ systems may manifest problems postoperatively in aneurysm clipping patients?

A. Medical Disease and Differential Diagnosis

A.1. What are the incidence, prevalence, and causes of subarachnoid hemorrhage (SAH) and what are the risk factors associated with rupture of intracranial aneurysms?

The prevalence of SAH is 2% to 5% with an incidence of 10 to 28 per 100,000 people. Each year, 25,000 cases of SAH occur in the United States, comprising 10% of all cases of stroke. Sixty percent of the cases occur in young individuals between the ages of 40 and 60. Therefore, a poor neurologic outcome is a devastating condition to be endured over a potentially long period.

Approximately one-third of patients die as a result of the acute bleed. Of the two-thirds who survive the acute bleed, one-half (one-third of total) later die or are severely disabled and half (one-third of total) have an acceptable outcome.

Cerebral aneurysms account for 75% to 80% of SAH; arteriovenous malformations are the cause in 4% to 5%, whereas no specific cause can be found in 15% to 20% of SAH. Other causes of SAH include trauma, mycotic aneurysm, sickle cell disease, cocaine use, and coagulation disorders.

Risk factors for rupture of cerebral aneurysms include hypertension, pregnancy, and vascular abnormalities (e.g., type III collagen deficiency and elastase abnormalities). One-third of patients with polycystic kidney disease have been found to have intracranial aneurysms at autopsy. Genetic predisposition plays a role: 7% of berry aneurysms are familial, and 5% to 10% of patients with ruptured aneurysm have a first-order relative with ruptured aneurysm. The rupture rate for aneurysm has been estimated at 0.14% per year for a 5-mm lesion to 1.1% per year for a 10-mm lesion.

Smoking and alcohol abuse also appear to predispose to aneurysm formation and rupture. Smoking at any time and female gender are related to the presence of multiple intracranial aneurysms, as well as accelerated aneurysm growth. Cocaine abuse and resultant episodic hypertension may predispose to aneurysmal rupture at an early age.

Death and disability are primarily due to the initial bleed, vasospasm, and rebleeding. Other causes include surgical complications, parenchymal hemorrhage, hydrocephalus, and complications of medical therapy.

Chang HS. Simulation of the natural history of cerebral aneurysms based on data from the International Study of Unruptured Intracranial Aneurysms. *J Neurosurg.* 2006;104:188–194.

Cotrell JE, Young WL, eds. *Cottrell and Young's Neuroanesthesia.* 5th ed. Philadelphia: Mosby Elsevier; 2010:218–246.

International Study of Unruptured Intracranial Aneurysms Investigators. Unruptured intracranial aneurysms: risk of rupture and risk of surgical intervention. *N Engl J Med*. 1998;339:1725–1733.

Juvela S, Pooras M, Poussa K. Natural history of unruptured intracranial aneurysms: probability and risk factors for aneurysm rupture. *J Neurosurg*. 2000;93:379–387.

Juvela S, Poussa K, Porras M. Factors affecting formation and growth of intracranial aneurysms: a long term follow-up study. *Stroke*. 2001;32:485–491.

Krex D, Schackert HK, Schackert G. Genesis of cerebral aneurysms: an update. *Acta Neurochir (Wien)*. 2001;143:429–448.

Tsutsumi K, Ueki K, Morita A, et al. Risk of rupture from incidental cerebral aneurysms. *J Neurosurg*. 2000;93:550–553.

Yoshimoto Y. A mathematical model of the natural history of intracranial aneurysm: quantification of the benefit of prophylactic treatment. *J Neurosurg*. 2006;104:195–200.

A.2. What are common sizes and locations of intracranial aneurysms?

Small (less than 12 mm) aneurysms make up 78% of the total, whereas large (12 to 24 mm) are 20%, and giant (greater than 24 mm) comprise 2%. Most aneurysms are located in the anterior circulation, with the junction of the anterior communicating and anterior cerebral arteries being the most common (39%). Thirty percent of aneurysms occur in the internal carotid artery, 22% in the middle cerebral artery, and 8% in the posterior circulation (posterior cerebral, basilar, and vertebral arteries).

Kasell NF, Torner JC, Haley C, et al. The international cooperative study on the timing of aneurysm surgery. Part 1. Overall management results. *J Neurosurg*. 1990;73:18–32.

Kasell NF, Torner JC, Haley C, et al. The international cooperative study on the timing of aneurysm surgery. Part 2. Surgical results. *J Neurosurg*. 1990;73:37–47.

A.3. What is the pathophysiology of aneurysmal rupture and SAH?

On the basis of experimental models, aneurysmal rupture leads to the leakage of arterial blood and a rapid increase in intracranial pressure (ICP), approaching diastolic blood pressure in the proximal intracerebral arteries. This increase in ICP causes a decrease in cerebral perfusion pressure (CPP) and a fall in CBF, leading to a loss of consciousness. The decrease in CBF diminishes bleeding and stops the SAH. A gradual reduction in ICP and an increase in CBF indicates improved cerebral function and possibly a return to consciousness. A persistent increase in ICP (perhaps resulting from thrombi in the cranial cisterns), however, indicates a persistent no-flow pattern with acute vasospasm, cell swelling, and death.

A.4. What are symptoms and signs of SAH?

Headache occurs in 85% to 95% of patients. Often, a brief loss of consciousness occurs, followed by diminished mentation; consciousness may be impaired to any degree or may be unaffected at the time of presentation. Symptoms may be similar to those of infectious meningitis (nausea, vomiting, and photophobia) secondary to subarachnoid blood. The patient may also experience motor and sensory deficits, visual field disturbances, and cranial nerve palsies. Finally, blood in the subarachnoid space may cause an elevated temperature.

Cotrell JE, Young WL, eds. *Cottrell and Young's Neuroanesthesia*. 5th ed. Philadelphia: Mosby Elsevier; 2010;218–246.

Guy J, McGrath BJ, Borel CO, et al. Perioperative management of aneurysmal subarachnoid hemorrhage. Part 1. Operative management. *Anesth Analg.* 1995;81:1060–1072.

A.5. How does one assess the severity of SAH?

Two grading scales are commonly used to assess neurologic status following SAH, the Hunt and Hess grade (Table 20.1) and the World Federation of Neurologic Surgeons' grade (Table 20.2), based on the Glasgow Coma Scale. The scales are useful in identifying a baseline neurologic status from which any acute changes should be assessed. In addition, the scales may correlate with physiologic status. Patients who are Hunt and Hess grades I and II have near-normal cerebral autoregulation and ICP.

Drake CG. Report of World Federation of Neurologic Surgeons Committee on a universal subarachnoid hemorrhage grading scale. *J Neurosurg.* 1988;68:985–986.

Hunt WE, Hess RM. Surgical risk as related to time of intervention in the repair of intracranial aneurysms. *J Neurosurg.* 1968;28:14–20.

A.6. What are the cardiovascular effects of SAH?

Injury to the posterior hypothalamus from SAH causes the release of norepinephrine from the adrenal medulla and cardiac sympathetic efferents. Norepinephrine can cause an increase in afterload and direct myocardial toxicity, leading to subendocardial ischemia. Pathologic analysis of myocardium of patients who have died of acute SAH has revealed microscopic subendocardial hemorrhage and myocytolysis.

Electrocardiographic abnormalities are present in 50% to 80% of patients with SAH. Most commonly, these involve ST segment changes and T wave inversions, but also include prolonged QT interval, U waves, and P wave changes. ST-T wave changes are usually scattered and not related to a particular distribution.

Dysrhythmias occur in 80% of patients, usually in the first 48 hours. Premature ventricular contractions are the most common abnormality, but any type of dysrhythmia is possible. They include severely prolonged QT interval, torsades de pointes, and ventricular fibrillation. In one series, 66% of the arrhythmias were considered mild,

Table 20.1 Modified Hunt and Hess Clinical Grades

GRADE[a]	CRITERIA
0	Unruptured aneurysm
I	Asymptomatic or minimal headache and slight nuchal rigidity
II	Moderate to severe headache, nuchal rigidity, but no neurologic deficit other than cranial nerve palsy
III	Drowsiness, confusion, or mild focal deficit
IV	Stupor, mild to severe hemiparesis, possible early decerebrate rigidity, vegetative disturbance
V	Deep coma, decerebrate rigidity, moribund appearance

[a] Serious systemic disease such as hypertension, diabetes, severe arteriosclerosis, chronic pulmonary disease, and severe vasospasm seen on arteriography result in placement of the patient in the next less favorable category.
From Hunt WE, Hess RM. Surgical risk as related to time of intervention in the repair of intracranial aneurysms. *J Neurosurg.* 1968;28:14–20, with permission.

Table 20.2 World Federation of Neurological Surgeons (WFNS) Grading Scale

WFNS GRADE	GLASGOW COMA SCALE	MOTOR DEFICIT
I	15	Absent
II	14–13	Absent
III	14–13	Present
IV	12–7	Present or absent
V	6–3	Present or absent

From Drake CG. Report of World Federation of Neurologic Surgeons Committee on a universal subarachnoid hemorrhage grading scale. *J Neurosurg.* 1988;68:985–986, with permission.

29% moderate, and 5% severe. In addition to increased catecholamine secretion, hypercortisolism and hypokalemia have been suggested as causes for the dysrhythmias seen with SAH.

Ventricular dysfunction, possibly leading to pulmonary edema, is present in approximately 30% of patients with SAH.

Cardiac troponin I predicts myocardial dysfunction in SAH with a sensitivity of 100% and a specificity of 91%. This compares with a sensitivity and specificity of 60% and 94% for CK-MB in predicting myocardial dysfunction. In order to plan optional anesthetic management, it would be important to determine if cardiac dysfunction is due to myocardial infarction or reversible neurogenic left ventricular dysfunction. A retrospective study from Duke determined that reversible neurogenic cardiac dysfunction was associated with a troponin level of 0.22 to 0.25 ng per mL and an ejection fraction of less than 40% by echocardiograms.

Bulsara KR, McGirt MJ, Liao L, et al. Use of peak troponin value to differentiate myocardial infarction from reversible neurogenic left ventricular dysfunction associated with aneurysmal subarachnoid hemorrhage. *J Neurosurg.* 2003;98:524–528.

Cotrell JE, Young WL, eds. *Cottrell and Young's Neuroanesthesia.* 5th ed. Philadelphia: Mosby Elsevier; 2010:218–246.

A.7. How is the diagnosis of SAH made?

Noncontrast CT scan can determine the magnitude and location of the bleed. It may also be useful in assessing ventricular size and aneurysm location. High-resolution CT (CT angiogram) with contrast can more precisely determine the location of the aneurysm.

Lumbar puncture can be used to diagnose SAH if CT is negative, especially when the patient presents more than 1 week after an initial bleed. Xanthochromia, a yellow discoloration of the cerebrospinal fluid (CSF) after centrifugation, is present from 4 hours to 3 weeks after SAH. The lumbar puncture can cause herniation or rebleeding. Therefore, a CT scan should be performed first if the patient presents within 72 hours of suspected SAH, once subarachnoid blood is confirmed.

Four-vessel angiography (right and left carotid and vertebral arteries) has been considered the gold standard in the diagnosis of intracranial aneurysm; however, CT angiography has been used with increasing frequency. The goal is to visualize all intracranial vessels, to localize the source of bleeding, and to rule out multiple aneurysms (5% to 33% of patients). Three-dimensional reconstructive angiograms and magnetic resonance angiography also may be used.

Guy J, McGrath BJ, Borel CO, et al. Perioperative management of aneurysmal subarachnoid hemorrhage. Part 1. Operative management. *Anesth Analg.* 1995;81:1060–1072.

Zhang L-J, Wu S-Y, Niu J-B, et al. Dual energy CT angiography in the evaluation of intracranial aneurysms: image quality, radiation dose, and comparison with 3D rotational digital subtraction angiography. *AJR.* 2010;194:23–30.

A.8. What is the risk for rebleeding for a patient with SAH?

The risk of rebleeding from a ruptured aneurysm is highest, 4%, in the first 24 hours after the initial bleed and 1.5% per day thereafter. Cumulative risk is 19% in 14 days and 50% at 6 months. After 6 months, the rebleeding risk is 3% per year.

Kassell NF, Torner JC. Aneurysmal rebleeding: a preliminary report from the Cooperative Aneurysm Study. *Neurosurgery.* 1983;13:479–481.

B. Preoperative Evaluation and Preparation

B.1. What are some concerns in going to the interventional neuroradiology suite in the midst of an angiogram to follow immediately with coiling of an aneurysm?

Whenever an anesthesiologist assumes care of a patient when the patient is already sedated, it may be more difficult to obtain an accurate medical history. In addition, the physical examination will be limited by the patient's position for the diagnostic study. Finally, the patient's capacity to consent may also be impaired by previous sedation.

B.2. What type of anesthesia is required for coiling of an aneurysm?

In most institutions, general anesthesia is required for coiling of an intracranial aneurysm. First, intraoperative neurologic testing is generally not required. Second, akinesis is very important not only when the coils are actually deployed but also while the interventionist is navigating the intracranial vessels to reach the aneurysm.

B.3. Would you proceed with induction of general anesthesia under these circumstances?

Yes, I would proceed. Obliteration of the aneurysm with coils has become the standard of care for basilar tip aneurysm, and it would be best for the patient to have this done in the same setting as the angiography, provided there were no contradictions to induction of general anesthesia (e.g., hemodynamic instability).

Cotrell JE, Young WL, eds. *Cottrell and Young's Neuroanesthesia.* St. Louis: Mosby; 2010:218–246.

Lee CZ, Young WL. Anesthetic considerations for interventional neuroradiology. *ASA Refresher Courses Anesthesiol.* 2005;33:145–154.

B.4. What types of emergencies can occur during coiling of an aneurysm and how should they be managed?

Basically, intraoperative emergencies can be divided into two categories—hemorrhage and thrombosis. Appropriate management requires constant communication between

the radiologist and surgeon and the anesthesiologist. If an intracranial hemorrhage occurs, the interventionalist may try to "glue" the hole in the aneurysm or embolize the parent vessel. If this is not possible, heparin should be rapidly reversed with protamine and a ventriculostomy will generally be placed by the surgical team. Management of $Paco_2$ can then be guided by the ICP. In the case of catheter-induced thrombosis, induced hypertension is usually desirable while tissue plasminogen activator or glycoprotein IIb/IIIa therapy is considered.

If a coil is malpositioned, anticoagulation would be continued while the interventional radiologist attempts to snare the coil. As in a thrombosis, it may be desirable to augment the blood pressure.

B.5. A craniotomy is planned for the following day to clip the middle cerebral artery aneurysm. Should surgery be postponed because of the patient's elevated creatinine phosphokinase (CPK) myocardial-bound (MB) fractions?

Fifty percent of patients will have an increase in CPK-MB fraction; however, CPK-MB per total CPK fraction is usually not consistent with transmural myocardial infarction. As discussed previously, troponin I levels are more sensitive. In addition, although some patients (0.7%) do sustain an myocardial infarction in the setting of SAH, little correlation is found between electrocardiographic abnormalities and ischemia in this population.

An echocardiogram may be useful in determining the severity of reversible neurogenic left ventricular dysfunction. If left ventricular function is found to be depressed, a pulmonary artery catheter or intraoperative transesophageal echocardiography may be helpful for intraoperative management.

The desire to delay surgery because of cardiac abnormalities must be weighed against the risk of rebleeding and vasospasm. In most cases, the risk of recurrent hemorrhage outweighs the risk of perioperative myocardial infarction. Furthermore, even if coronary artery disease is present, these patients are not candidates for angioplasty or myocardial revascularization, which requires heparinization. If pulmonary edema or malignant dysrhythmias are present, it may be prudent to postpone surgery until such problems are controlled medically. However, if these problems are not present, then clipping of the aneurysm may be indicated. Bulsara et al. found that 2.9% of patients had severe cardiac dysfunction. In this study, neurogenic left ventricular dysfunction resolved over 4 to 5 days.

Bulsara KR, McGirt MJ, Liao L, et al. Use of peak troponin value to differentiate myocardial infarction from reversible neurogenic left ventricular dysfunction associated with aneurysmal subarachnoid hemorrhage. *J Neurosurg.* 2003;98:524–528.

B.6. Would you premedicate this patient before craniotomy?

No. When the patient is in a Hunt and Hess grade III to V state, anxiety is unlikely. Furthermore, heavy sedation may decrease ventilation, raising $Paco_2$ and increasing CBF and ICP, which, at the very least, may hinder preoperative and postoperative neurologic evaluation. If patients are Hunt and Hess grade I to II and it appears that preoperative anxiety might lead to hemodynamic instability, a small dose of benzodiazepine may be appropriate.

Medications such as calcium channel blockers (nimodipine), anticonvulsants, and corticosteroids should be continued preoperatively on the day of surgery.

If the patient is at risk for aspiration, medications to decrease gastric acidity and volume are appropriate. Most patients will already be receiving a histamine-2 blocker if they are on dexamethasone.

Cotrell JE, Young WL, eds. *Cottrell and Young's Neuroanesthesia.* 5th ed. Philadelphia: Mosby Elsevier; 2010:218–246.

C. Intraoperative Management

C.1. What are the goals of the induction and maintenance of anesthesia for this patient?

The primary goal is to prevent aneurysm rupture on induction or intraoperatively while maintaining adequate CPP. The goal of matching anesthetic depth to surgical stimulation is more important than which specific drugs are used. In general, the anesthesiologist should provide for rapid and reversible titration of blood pressure, maintain CPP, and protect against cerebral ischemia. An additional goal is to provide a relaxed brain for ease of surgical exposure with minimal brain retraction. Finally, the anesthetic should be planned to achieve a rapid, smooth emergence, allowing prompt neurologic assessment. This can be accomplished with a combination of balanced anesthesia, muscle relaxation, and sympathetic blockers.

Bendo AA. Intracranial vasculary surgery. *Anesthesiol Clin North Am.* 2002;20:377–388.

Cotrell JE, Young WL, eds. *Cottrell and Young's Neuroanesthesia.* 5th ed. Philadelphia: Mosby Elsevier; 2010:218–246.

C.2. Is placement of an arterial line necessary for induction of anesthesia in this patient in the interventional neuroradiology suite?

In this case, because a femoral sheath is in place at the time that anesthesia is being induced, one may transduce femoral arterial pressure during induction. However, because the patient has two aneurysms and because the sheath will be removed at the end of the procedure, it would be prudent to place an additional arterial line at some point before removal of the sheath. When a large coaxial catheter is placed through the femoral sheath, systolic pressure is underestimated. The mean pressure, though, should be accurate. Recent studies have suggested that placement of an arterial line for induction is not essential when an unruptured aneurysm is to be coiled. At Weill Cornell Medical Center, we do not usually place an arterial line before induction for embolization of unruptured aneurysm.

Cotrell JE, Young WL, eds. *Cottrell and Young's Neuroanesthesia.* 5th ed. Philadelphia: Mosby Elsevier; 2010:247.

Lai YC, Manninen PH. Anesthesia for cerebral aneurysms: a comparison between interventional neuroradiology and surgery. *Can J Anaesth.* 2001;48:391–395.

C.3. How would you assess fluid status in this patient?

Several issues in interventional radiology complicate fluid management. First, contrast material acts as an osmotic diuretic. Often, these patients have had a CT scan with contrast before the angiograms and may become intravascularly depleted. Second, the femoral sheath and other catheters are constantly flushed with a heparinized saline solution. It is not uncommon for a patient to receive 1,000 mL or more of flush fluid during the case. This must be taken into account when calculating fluid balance.

C.4. Would monitoring central venous pressure (CVP) be useful in this patient for craniotomy for clipping?

Many have suggested that CVP monitoring is essential in assessing volume replacement needs because urine output will be affected by osmotic or loop diuretics administered to facilitate surgical exposure. In addition, should vasoactive medication become necessary, it may be most effectively administered through a central venous catheter.

One disadvantage of CVP placement in the neurosurgical patient is catheter placement. Some clinicians are concerned that placement of an internal jugular venous CVP will compromise venous outflow of the head, thereby predisposing to bleeding or brain swelling, though this remains controversial. A "long-arm" or antecubital CVP line may be more difficult to insert and have a higher incidence of thrombophlebitis. Multiple studies have shown the complication rate of central catheter placement to be as high as 14%. When including failure to place the catheter, the complication rate rises to 54%. Nevertheless, use of an ultrasound-guided approach to placement of central venous catheters reduces the complication rates to less than 2% to 5% and should be the standard of care whenever possible.

Finally, a poor correlation between CVP and left ventricular end-diastolic pressure has been documented in SAH, so a pulmonary artery catheter may be more useful in assessing volume status as well as providing a monitor of cardiac output in those patients who have had preoperative cardiac problems. Patients who are expected to be candidates for hypertensive hypervolemic hemodilution therapy for vasospasm or for barbiturate coma may also benefit from placement of a pulmonary artery catheter.

Central pressure monitoring is usually instituted after the patient is asleep to minimize stress to the patient. One should be careful to use the minimal degree of head-down tilt necessary to access the central circulation, because a severe Trendelenburg position may have deleterious effects on ICP and CPP.

In view of this evidence, at our institution, we reserve placements of CVP and pulmonary artery catheters for those patients who have documented cardiac dysfunction or if we are unable to secure large-bore peripheral intravenous access. Volume status may be assessed by noninvasive monitors or by careful assessment of the arterial waveform.

Akmal AH, Hasan M, Mariam A. The incidence of complications of central venous catheters at an intensive care unit. *Ann Thorac Med.* 2007;2:61–63.

Eisen LA, Narasimhan M, Berger JS, et al. Mechanical complications of central venous catheters. *J Intensive Care Med.* 2006;21:40–46.

Marik PE, Cavallazzi R, Vasu T, et al. Dynamic change in arterial waveform derived variables and fluid responsiveness in mechanically ventilated patients: a systematic review of the literature. *Crit Care Med.* 2009;37:2642–2647.

C.5. What other forms of monitoring would you consider?

Electroencephalography (EEG) and somatosensory evoked potentials (SSEPs) have been advocated by some authors, though they are not standard monitoring in most hospitals. Although EEG has been used to monitor cerebral ischemia, scalp electrodes may not reflect activity of brain areas most at risk. Cortical electrodes, such as those used in epilepsy surgery, may avoid the problem of attenuation of the scalp electroencephalographic signal by CSF drainage and air between scalp electrodes and brain surface during surgery. EEG is useful in titrating barbiturate or propofol infusion if burst suppression is desired during temporary clipping.

SSEPs may detect reversible ischemia during temporary vessel occlusion, but they may not detect ischemia in subcortical structures and motor cortex. Furthermore, SSEPs have relatively high false-positive (38% to 60%) and false-negative (5% to 34%) rates. Brainstem auditory evoked responses may be useful in monitoring during posterior circulation aneurysm clipping. Motor evoked potentials may be superior in

detecting subcortical ischemia. The use of SSEP and motor evoked potential monitoring usually warrants the use of total intravenous anesthesia and elimination of muscle relaxants from the anesthetic.

Microvascular Doppler ultrasound evaluation may detect inadvertent vessel occlusion, but it cannot assess for adequacy of collateral perfusion.

Monitoring of ICP is common, with the probability of increased ICP greatest at 24 to 48 hours after SAH. An intraventricular catheter not only allows for ICP monitoring but also allows for CSF drainage to improve operating conditions. If an intraventricular catheter is not present, lumbar spinal drain may be placed. One must be careful not to allow substantial CSF drainage before dural opening because this may decrease ICP allowing for an increase in transmural pressure and possible rupture.

Intraoperative angiography is one means by which to ensure complete obliteration of the aneurysm without clip occlusion of the parent artery or perforating branches. Use of this modality may increase with the installation of more "hybrid" operating rooms, which are fully equipped with advanced angiography equipment in the operating room suite.

Horiuchi K, Suzuki K, Sasaki T, et al. Intraoperative monitoring of blood flow insufficiency during surgery of middle cerebral artery aneurysms. *J Neurosurg.* 2005;103:275–283.

Neulogh G, Schramm J. Monitoring of motor evoked potentials compared with somatosensory evoked potentials and microvascular Doppler ultrasonography in cerebral aneurysm surgery. *J Neurosurg.* 2004;100;389–399.

Szelenyi A, Langer D, Kothbauer K, et al. Monitoring of muscle motor evoked potentials during cerebral aneurysm surgery: intraoperative changes and postoperative outcome. *J Neurosurg.* 2006:105:675–681.

C.6. What are your particular concerns during induction of anesthesia in this patient?

If an aneurysm ruptures during anesthetic induction, mortality is high (approximately 75%). Therefore, precise control of transmural pressure is important in preventing aneurysm rupture.

$$\text{Transmural pressure} = \text{CPP} = \text{MAP} - \text{ICP or CVP (whichever is greater)},$$
where MAP = mean arterial pressure

On the other hand, one does not want CPP to be so low that ischemia develops, especially in areas of vasospasm.

Tsementzis SA, Hitchcock ER. Outcome from "rescue clipping" of ruptured intracranial aneurysms during induction of anesthesia and endotracheal intubation. *J Neurol Neurosurg Psychiatry.* 1985;48:160–163.

C.7. How would you accomplish a smooth and safe induction and intubation of this patient?

Assuming that evaluation of the airway indicated that intubation would not be difficult, one would begin with preoxygenation. Thiopental 3 to 5 mg per kg, propofol 1.5 to 2.5 mg per kg, and etomidate 0.5 to 1 mg per kg have similar effects on CBF and cerebral metabolic rate. Given that this patient had no other medical problems, thiopental is a reasonable choice. One may want to avoid ketamine for induction because of its associated increase in CBF and ICP.

After loss of consciousness and apnea, care must be taken to maintain a normal $Paco_2$ and avoid extreme hyperventilation. Vigorous hyperventilation will lower $Paco_2$,

decreasing CBF. This may lower ICP to such a degree that if MAP is maintained or increased, transmural pressure may be increased, leading to rupture of the aneurysm.

A nondepolarizing muscle relaxant, which has no effect on ICP or CBF, should be added to facilitate intubation. The neuromuscular junction should be monitored to ensure that paralysis is adequate to avoid coughing with intubation.

Fentanyl 3 to 5 μg per kg, sufentanil 0.5 to 1 μg per kg, or remifentanil 0.25 to 1 μg per kg can be added 3 to 5 minutes before laryngoscopy to blunt the hemodynamic response. Isoflurane, desflurane, or sevoflurane is added to deepen the anesthetic. Finally, approximately 90 seconds before laryngoscopy, lidocaine 1.5 to 2 mg per kg or esmolol 0.5 mg per kg can be added to further blunt the hemodynamic response to intubation.

Lidocaine decreases both CBF and cerebral metabolic rate for oxygen, and at high concentrations, it can cause seizures. Esmolol and labetalol have no effect on CBF and ICP, even in brain areas where autoregulation may not be intact. Extreme reductions in MAP (greater than 35%) may compromise CPP in patients with increased ICP.

Cotrell JE, Young WL, eds. *Cottrell and Young's Neuroanesthesia*. 5th ed. Philadelphia: Mosby Elsevier; 2010:218–246.

C.8. Would you perform a rapid-sequence induction and intubation on this patient?

No indication is seen for a rapid-sequence induction and intubation in this patient. Overall risk of aspiration during general anesthesia has been estimated at 0.05%; nevertheless, the risk of aneurysm rupture during induction is 1% to 2%. Therefore, unless a clear indication exists for rapid-sequence induction, it is best avoided.

If rapid-sequence induction is indicated, one may consider using vecuronium 0.15 to 0.20 mg per kg or rocuronium 0.9 mg per kg rather than succinylcholine. Succinylcholine may cause an increase in ICP, although this increase can be attenuated or eliminated by deep anesthesia or prior defasciculation. Succinylcholine, more importantly, may lead to hyperkalemia and possibly ventricular fibrillation in those patients presenting with motor deficits following SAH.

In the case of a full stomach or an anticipated difficult airway, careful awake fiber-optic intubation, with use of appropriate sedation and topical application of local anesthesia, is an appropriate alternative. Under such circumstances, it is useful to have an assistant so that while one person is securing the airway, the other is solely focused on controlling the hemodynamics with titration of appropriate medication.

Cotrell JE, Young WL, eds. *Cottrell and Young's Neuroanesthesia*. 5th ed. Philadelphia: Mosby Elsevier; 2010:218–246.

Guy J, McGrath BJ, Borel CO, et al. Perioperative management of aneurysmal subarachnoid hemorrhage. Part 1. Operative management. *Anesth Analg*. 1995;81:1060–1072.

Iwasuta N, Kuroda N, Amaha K, et al. Succinylcholine induced hyperkalemia in patients with ruptured central aneurysms. *Anesthesiology*. 1980;53:64–67.

Lanier WL, Milde JH, Michenfelder JD. Cerebral stimulation following succinylcholine in dogs. *Anesthesiology*. 1986;64:551–559.

Olsson GL, Hullen B, Hambraeus-Johnzonk K. Aspiration during anesthesia: a computer-aided study of 185,838 anesthetics. *Acta Anesthesiol Scand*. 1986;30:84–92.

Stirt JA, Grosslight KR, Bedford RF, et al. Defasciculation with metocurine prevents succinylcholine associated increases in intracranial pressure. *Anesthesiology*. 1987;67:50–53.

Tsementzis SA, Hitchcock ER. Outcome from "rescue clipping" of ruptured intracranial aneurysms during induction of anesthesia and endotracheal intubation. *J Neurol Neurosurg Psychiatry*. 1985;48:160–163.

C.9. What are the effects of hypoxemia and hypercapnia, such as would be seen with loss of the airway on induction, on cerebral blood flow (CBF)?

Each millimeter of mercury increase in $Paco_2$ increases CBF 3% to 4%, when $Paco_2$ is in the range of 20 to 80 mm Hg. In addition, the hypoxia that will ensue if the airway is not secured in a timely manner will also cause an increase in CBF once Pao_2 is less than 60 mm Hg (Fig. 20.1).

C.10. What is optimal fluid management for aneurysm clipping? Would you use a dextrose-containing solution?

Maintenance fluid requirements and blood loss should be replaced. One wants to avoid profound hypovolemia not only for its detrimental cardiovascular effects but also because it is associated with cerebral ischemia and perioperative neurologic deficits resulting from vasospasm. Some authors advocate mild hypervolemia to maximize cerebral CBF and minimize vasospasm; however, one must keep in mind the possibility of cerebral edema as well as acute congestive heart failure.

In general, dextrose-containing solutions should be avoided because an increased incidence of neurologic deficits associated with glucose administration has been found in experimental models of focal cerebral ischemia. At Weill Cornell Medical Center, we try to maintain blood glucose less than 180 mg per dL.

Use of crystalloid versus colloid for fluid management and which type of crystalloid solution, lactated Ringer's solution versus normal saline or Normosol, has long been a matter of controversy. Although some authors advocate colloid solutions to diminish the risk of brain swelling, no evidence exists that the solution may predispose to brain edema and contribute to hyponatremia, which may increase the incidence of delayed ischemic neurologic deficits. Therefore, normal saline is the fluid of choice.

A moderate degree of hemodilution to a hematocrit of 30% to 35% usually lowers blood viscosity, thereby increasing CBF. The goal is to increase oxygen delivery by increasing CBF, without allowing the hematocrit to decrease to the degree that reduction in oxygen content negates the increase in CBF. Hematocrit, serum sodium, and serum osmolality measurements may be followed to guide fluid therapy. Serum sodium should be maintained within normal limits, both to maintain serum oncotic pressure and to avoid the hyponatremia associated with cerebral salt wasting.

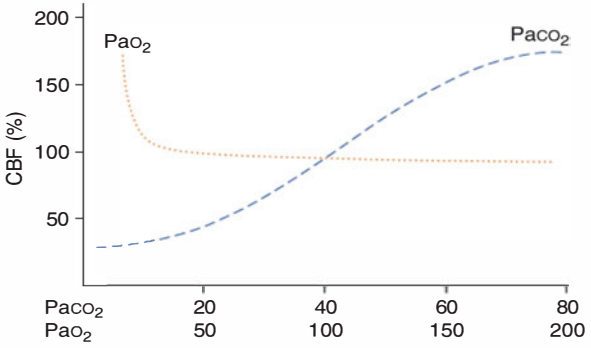

Figure 20.1 Change in cerebral blood flow as a function of arterial carbon dioxide ($Paco_2$) and oxygen (Pao_2) tension. CBF, cerebral blood flow. (From Albin MS, ed. *Textbook of Neuroanesthesia: With Neurosurgical and Neuroscience Perspectives.* New York: McGraw-Hill; 1997:30, with permission.)

Guy J, McGrath BJ, Borel CO, et al. Perioperative management of aneurysmal subarachnoid hemorrhage. Part 1. Operative management. *Anesth Analg.* 1995;81:1060–1072.

Lanier WL, Stangland KJ, Scheithauer BW, et al. The effects of dextrose infusion and head position on neurologic outcome after complete cerebral ischemia in primates: examination of a model. *Anesthesiology.* 1987;66:39–48.

Maroon JC, Nelson PB. Hypovolemia in patients with subarachnoid hemorrhage: therapeutic implications. *Neurosurgery.* 1979;4:223–226.

McGirt MJ, Blessing R, Ninjee SM, et al. Correlation of serum brain natriuretic peptide with hyponatremia and delayed ischemic neurologic deficits after subarachnoid hemorrhage. *Neurosurgery.* 2004;54:1369–1374.

C.11. After the bone plate was removed and as the dura was being opened, the surgeon complained that the brain was "tight." What could you do to achieve better brain relaxation and facilitate surgical exposure?

Any method that rapidly decreases ICP before dural opening may suddenly increase transmural pressure and lead to aneurysm rupture. After dural opening, one of the fastest ways to decrease cerebral blood volume and improve exposure is through hyperventilation. Mild hypocarbia ($Paco_2$ = 30 to 35 mm Hg) can usually be established before dural opening, with moderate hypocarbia ($Paco_2$ = 25 to 30 mm Hg) after dural opening. Because of the risk for cerebral ischemia secondary to diminished CBF, normocarbia should be maintained whenever possible in patients with vasospasm.

Mannitol is the most frequently used diuretic at our institution. It is given as an infusion for a total dose of 0.7 g per kg (0.25 to 1 g per kg). Its immediate effect is a transient rise in intravascular volume, which may pose problems in patients with impaired ventricular function. In addition, too rapid infusion can lead to decreases in systemic vascular resistance. Its onset of diuretic action is in 10 to 15 minutes, with peak effect occurring at 60 to 90 minutes. If mannitol does not produce the desired brain relaxation and the serum osmolality is greater than 320 mOsm, additional mannitol is unlikely to produce additional effect. In those patients who may not tolerate the initial effects of mannitol, intravenous furosemide 0.1 to 0.3 mg per kg can be substituted. Both medications can cause derangements in fluid status and serum electrolytes that require close monitoring.

Drainage of CSF from either a lumbar drain or an intraventricular catheter is usually effective in optimizing surgical exposure. One must be careful to avoid significant CSF drainage before dural opening to prevent either brainstem herniation or a sudden decrease in transmural pressure. Similarly, hemodynamic instability can ensue if CSF is drained too rapidly at any point in the operation.

If tight brain remains a problem, one must ascertain that there is no hypoxemia or hypercarbia. In addition, one should consider eliminating N_2O if it is in use and reducing the amount of volatile anesthetic, because all inhalational agents are cerebral vasodilators and may potentially increase ICP. Of course, if inhaled agents are reduced, appropriate intravenous agents should be substituted to ensure adequate anesthesia.

One may give a bolus of thiopental to decrease $CMRo_2$ and CBF; nevertheless, one must maintain MAP to maintain CPP. At the time of patient positioning, one must ensure that no impediment exists to venous outflow of the brain (i.e., that extreme flexion or rotation of the head is avoided and that no monitor cables [electrocardiogram] leads are draped across the neck).

Bendo AA. Intracranial vascular surgery. *Anesthesiol Clin North Am.* 2002;20:377–388.

Cotrell JE, Young WL, eds. *Cottrell and Young's Neuroanesthesia.* 5th ed. Philadelphia: Mosby Elsevier; 2010:218–246.

Sullivan HG, Keenan RL, Isrow L. The critical importance of $PaCO_2$ during intracranial aneurysm surgery. *J Neurol Neurosurg.* 1980;52:426–431.

C.12. How might transmural pressure be decreased to allow for aneurysm clip placement?

The most widely accepted method for producing a slack aneurysm to allow for clip placement is the use of temporary clip occlusion of one or more parent vessels. For example, to place a permanent clip on an anterior communicating artery aneurysm, a temporary clip can be placed on either the right or left anterior cerebral artery or both. Advantages of temporary clip use include a greater reduction in transmural pressure and greater ease in clipping, decreased incidence of intraoperative rupture, and avoidance of controlled hypotension.

The maximal duration of temporary clip application before a neurologic deficit occurs is unknown, but it is probably related to the location of the aneurysm and distribution of perforating vessels distal to the temporary clip. White matter and major deep nuclei are likely to be more susceptible than gray matter to temporary ischemia. Risk factors for neurologic deficit following temporary clip placement include poor preoperative neurologic condition, age older than 61 years, and distribution of perforating arteries in distal basilar and horizontal segments of middle cerebral artery.

Akyuz AA, Erylmaz M, Ozdemir C, et al. Effect of temporary clipping on frontal lobe functions in patients with ruptured aneurysm of the anterior communicating artery. *Acta Neurochir Scan.* 2005;112:293–297.

Kett-White R, Hutchinson PJ, Al-Ravie PG, et al. Cerebral oxygen and microdialysis monitoring during aneurysm surgery: effects of blood pressure, cerebral spinal fluid drainage and temporary clipping on infarction. *J Neurosurgery.* 2002;96:1013–1019.

C.13. What is the purpose of controlled hypotension and how is it achieved?

In the past, controlled hypotension was used to decrease transmural pressure, making the aneurysm neck slack enough to allow placement of a clip without vessel rupture. Various agents were used to achieve controlled hypotension, including volatile agent, nitroprusside, esmolol, labetalol, nitroglycerin, and trimethaphan. Specific agents were selected based on the patient's pre-existing medical conditions, especially coronary ischemia or poor ventricular function. In an otherwise healthy patient, sodium nitroprusside infusion may be used for its rapid onset, easy titratability, and quick offset. An esmolol infusion can be added to augment hypotension and counteract the reflex tachycardia and cyanide toxicity seen with nitroprusside. Side effects of nitroprusside include cyanide toxicity, rebound hypertension, and intrapulmonary shunting. Direct measurement of CVP is useful when planning to use controlled hypotension in these patients.

During controlled hypotension, MAP is usually maintained at a minimum of 50 mm Hg in previously normotensive individuals. Neurologic function monitors (EEG, SSEP, brainstem auditory evoked response, and cerebral oximetry) may be useful in guiding target level of MAP.

Albin MS, ed. *Textbook of Neuroanesthesia: With Neurosurgical and Neuroscience Perspectives.* New York: McGraw-Hill; 1997:877–878.

Ornstein E, Young WL, Ostapkovich N, et al. Deliberate hypotension in patients with intracranial arteriovenous malformations: esmolol compared with isoflurane and sodium nitroprusside. *Anesth Analg.* 1991;72:639–644.

C.14. What are some of the drawbacks of controlled hypotension?

The main drawback of controlled hypotension is that it leads to a global decrease in CPP. CPP is then further diminished in the presence of vasospasm or in areas of brain retraction. In a retrospective study, multiple regression analysis indicated that

patients who underwent even limited periods of controlled hypotension had a worse outcome, both in terms of Glasgow Outcome Scale (multiple regression) and higher incidence and severity of vasospasm. At Weill Cornell Medical Center, we avoid controlled hypotension in neurosurgery.

Chang HS, Hongo K, Nakagawa H. Adverse effects of limited hypotensive anesthesia on the outcome of patients with subarachnoid hemorrhage. *J Neurosurg.* 2000;92:971–975.

Ruta TS, Mutch WAC. Controlled hypotension for cerebral aneurysm surgery: are the risks worth the benefits? *J Neurosurg Anesthesiol.* 1991;3:153–156.

C.15. What methods of cerebral protection might you use during this operation?

Cerebral protection has long been a matter of much investigation and controversy. Barbiturate loading has been shown in animals to be protective against focal ischemia, though no controlled human studies have been performed. Barbiturates decrease cerebral metabolic rate for glucose and oxygen and lower CBF and ICP. The dose is usually titrated to electroencephalographic silence or burst suppression. At doses used to suppress electroencephalographic activity, the patient may experience cardiovascular depression. The dose of barbiturate traditionally used for cerebral protection may also prolong emergence and hinder postoperative neurologic evaluation. Although barbiturates were originally thought to protect against ischemia through metabolic depression, other factors such as redistribution of blood flow to ischemic areas, blockade of the sodium channels and glutamate receptors, attenuation of *N*-methyl D-aspartate (NMDA) and α-amino-3-hydroxy-5-methyl- 4-isoxazole propionic acid (AMPA)-mediated glutamate toxicity all play a role.

Propofol has also been used as an alternative to thiopental sodium. Cerebral protection from propofol is thought to result from scavenging of free radicals, inhibition of glutamate release, and prevention of lipid peroxidation. In studies involving both volatile anesthetics and propofol, apoptotic cell death is delayed, but not prevented, if the ischemic result is mild.

Etomidate decreases cerebral metabolic rate at electroencephalographic burst suppression and prevents an increase in excitatory neurotransmitters during cerebral ischemia in animal models; nevertheless, it has been associated with a greater volume of injured brain than thiopental and control groups in focal ischemia in hypertensive rats.

Deliberate mild hypothermia (32.5° C to 35.5° C), although promising in animal models, did not demonstrate efficacy with patients with good-grade aneurysm in the Intraoperative Hypothermia for Aneurysm Surgery Trial (IHAST) 2. Magnesium has been proposed as a cerebroprotective agent during aneurysm clipping. Magnesium is a cerebral vasodilator that, in animal models, blocks voltage-dependent calcium channels and reverses experimental vasospasm. In humans, magnesium has been found to attenuate brain tissue hypoxia during temporary occlusion. Finally, erythropoietin is being investigated as a cerebroprotectant.

Chan MTV, Boet R, Ng SCP, et al. Magnesium sulfate for brain protection during temporary cerebral artery occlusion. *Acta Neurochir.* 2005;95(suppl):107–111.

Drummond JC, Cole DJ, Patel PM, et al. Focal cerebral ischemia during anesthesia with etomidate, isoflurane, or thiopental: a comparison of the extent of cerebral injury. *Neurosurgery.* 1995;37:742–748.

Engelhard K, Werner C, Eberspacher E, et al. Influence of propofol on neuronal damage and apoptotic factors after incomplete cerebral ischemia and reperfusion in rats: a long-term observation. *Anesthesiology.* 2004;101:912–917.

Engelhard K, Werner C, Hoffman WE, et al. The effect of sevoflurane and propofol on cerebral neurotransmitter concentrations during cerebral ischemia in rats. *Anesth Analg.* 2003;97:1155–1161.

Guy J, McGrath BJ, Borel CO, et al. Perioperative management of aneurysmal subarachnoid hemorrhage. Part 1. Operative management. *Anesth Analg.* 1995;81:1060–1072.

Kawaguchi M, Furuya H, Patel PM. Neuroprotective effects of anesthetic agents. *J Anesth.* 2005;19:150–156.

Liu R, Suzuki A, Guo Z, et al. Intrinsic and extrinsic erythropoietin enhances neuroprotection against ischemia and reperfusion injury in vitro. *J Neurochem.* 2006;96:1101–1110.

Ravussin P, Detribolet N. Total intravenous anesthesia with propofol for burst suppression in cerebral aneurysm surgery: a preliminary report of 42 patients. *Neurosurgery.* 1990;32:236–240.

Warner DS, Takaoka S, Wu B, et al. Electroencephalographic burst suppression is not required to elicit maximal neuroprotection from pentobarbital in a rat model of focal cerebral ischemia. *Anesthesiology.* 1996;84:1475–1484.

C.16. Would you induce mild hypothermia as a means of cerebral protection?

Hypothermia causes a greater reduction in cerebral metabolic rate for glucose and oxygen than the level attained at electroencephalographic silence because its reduction of metabolism is caused by a reduction in both neuronal electrical activity and enzyme activity related to maintenance of cellular function. Hypothermia also reduces the release of excitatory neurotransmitters. Significant reduction in infarct size after global and focal ischemia has been demonstrated in several animal studies. Unfortunately, these advantages have not been documented in clinical trial. The IHAST study showed no differences in Glasgow Outcome Scale at 3 months in patients at good grade.

Disadvantages of unintentional hypothermia documented in the literature include an increased incidence of myocardial ischemia in peripheral vascular surgery, increased incidence of postoperative wound infection in abdominal surgery, coagulopathy, prolonged drug clearance, and hyperglycemia. In the IHAST study, the hypothermic group had a small increase in infection rate. As a result of IHAST, we no longer deliberately induce hypothermia in patients at good grade for aneurysm clippings.

Frank SM, Beattie C, Christopherson R, et al. Unintentional hypothermia is associated with postoperative myocardial ischemia. *Anesthesiology.* 1993;78:468–476.

Kurz A, Sesler DI, Lenhardt R, et al. Perioperative normothermia to reduce the incidence of surgical wound infection and shorten hospitalization. *N Engl J Med.* 1996;334:1209–1215.

Todd MM, Handman BJ, Clarke WR, et al. Intraoperative hypothermia for aneurysm surgery trial. *N Engl J Med.* 2005;352:135–145.

C.17. What are the indications for deep hypothermic circulatory arrest?

Hypothermic circulatory arrest at body temperature less than 22° C (71.6° F) is reserved for giant aneurysms, difficult basilar artery aneurysms, and anatomically complex aneurysms that are not clippable without complete cessation of blood flow and are not amenable to the use of temporary clips. Deep hypothermic circulatory arrest requires cooperation between several services, including anesthesiology, neurosurgery, cardiac surgery, and perfusionists. In addition to the concerns mentioned regarding anesthesia for the person with an intracranial aneurysm and the need for prompt awakening for ease of neurologic assessment, deep hypothermic circulatory arrest adds concerns regarding institution of and separation from cardiopulmonary

bypass, systemic heparinization and protamine reversal, and, of course, rewarming from profound hypothermia. This is rarely performed now that coil embolization is possible for many of these aneurysms.

Young WL, Lawtom MI, Gupta DK, et al. Anesthetic management of deep hypothermic circulatory arrest for cerbral aneurysm clipping. *J Neurosurg Anesthesiol.* 2003;15: 274–277.

C.18. What steps should be taken in the case of intraoperative rupture of an intracranial aneurysm?

The incidence of intraoperative rupture is 2% to 19%. The stage of the operation at which rupture occurs affects outcome, with rupture at induction being the worst. After induction, the most common times for rupture are when the dura mater or arachnoid mater are being opened, during intracranial hematoma removal, and, of course, during dissection exposure of the aneurysm. At any point in the operation, a sudden sustained increase in blood pressure with or without bradycardia is suggestive of rupture. If rupture is suspected on induction, one must institute measures to control ICP while maintaining CPP.

If rupture occurs during surgical dissection, mortality is lower. The primary concern is to control bleeding while maintaining systemic perfusion. Bleeding is controlled by placement of temporary clips or by clamping or compression of the ipsilateral carotid artery in the neck if the aneurysm is too proximal. If bleeding is not controlled in a timely manner and a significant amount of blood accumulates in the subarachnoid space, severe brain swelling that is refractory to all treatment may develop. At Weill Cornell Medical Center, we do not use controlled hypotension at any point in the surgery even in the face of intraoperative rupture.

Hawkin K, Kuroda S, Takahashi A, et al. Intraoperative premature rupture of the cerebral aneurysms: analysis of the causes and management. *Acta Neurochir (Wien).* 1999;141: 1255–1263.

C.19. How would you plan the emergence from an anesthetic for aneurysm clipping?

The goal is to have a patient comfortable and not coughing or straining or subject to hypercarbia or wide variations in blood pressure.

After discontinuing all anesthetic agents and reversing neuromuscular blockade, the use of a lidocaine 1.5-mg per kg bolus may minimize bucking and reaction to the endotracheal tube. Strict control of blood pressure must be observed especially in the presence of ischemic heart disease or in patients suspected of having multiple aneurysms. One should keep the blood pressure within 20% of the patient's normal measurement.

D. Postoperative Management

D.1. Would you extubate the patient postoperatively?

Most patients who are in Hunt and Hess grades I and II can be extubated postoperatively with no need for airway support. Patients in grades IV and V usually require mechanical ventilation postoperatively, whereas grade III patients may or may not require intubation and mechanical ventilation. Patients with vertebral or basilar

artery aneurysms may require airway protection secondary to cranial nerve damage and loss of protective reflexes.

If this patient was able to follow commands, was clinically recovered from the effects of muscle relaxants, and had established an adequate ventilatory pattern with return of protective airway reflexes, extubation would be appropriate.

Bendo AA. Intracranial vascular surgery. *Anesthesiol Clin North Am.* 2002;20:377–388.

D.2. What would be the differential diagnosis if the patient did not return to her preoperative neurologic condition?

If the patient had a focal neurologic deficit on awakening in the operating room, the cause most likely would be a surgical one, although new-onset vasospasm is also a possibility.

If the patient failed to awaken, the first step would be to ensure that all inhalational and infused anesthetics had been discontinued. Second, one should make sure that neuromuscular blockade was fully reversed. One should make sure that the patient had been appropriately rewarmed, because hypothermia would prolong the duration of action of most intravenous medications. While considering reversal of benzodiazepines and narcotics, one should rule out other causes such as hypoxia, hypercarbia, hyponatremia, and hypoglycemia. One should consider the possibility of intraoperative seizure, with delayed emergence resulting from a postictal state. If after reversal of all anesthetic agents the patient had not awakened, a CT scan should be obtained to rule out subdural hematoma, intracranial hemorrhage, hydrocephalus, and pneumocephalus. An angiogram may also be obtained to rule out vascular occlusion. An electroencephalogram might be appropriate to rule out subconvulsive status epileptics.

Cotrell JE, Young WL, eds. *Cottrell and Young's Neuroanesthesia.* 5th ed. Philadelphia: Mosby Elsevier; 2010:218–246.

D.3. On postoperative day 2, the patient became disoriented and developed hemiplegia. A CT scan was obtained, which shows no new intracranial bleeding. What other diagnostic studies should be performed?

If transcranial Doppler is available, an increased value for cerebral arterial flow velocity would be suggestive for vasospasm, leading to delayed cerebral ischemia. Tissue oximetry may also be useful as a monitor for vasospasm. Angiography is the gold standard for the diagnosis of cerebral vasospasm and should be performed to confirm the diagnosis and characterize the number and location of the vessels involved.

Cerebral vasospasm may be localized to the area of aneurysm rupture or in an area of the brain remote from SAH. The worst prognosis is in those patients in whom vasospasm is diffuse. Of course, as these studies are being done, laboratory values should be checked to make sure no new or worsening metabolic derangement is contributing to the neurologic deterioration.

D.4. What is cerebral vasospasm and what causes it?

Vasospasm, which occurs in 35% of patients with SAH, is a segmental or diffuse narrowing of the lumen of one or more intracranial arteries. It is the most common cause of delayed cerebral ischemia and may be seen angiographically in 60% of patients, even if clinical manifestations are not apparent.

The severity of vasospasm is apparently related to the amount and location of subarachnoid blood. Injection of blood into the subarachnoid space causes vasospasm in experimental animals and antifibrinolytics apparently worsen the spasm. On a molecular level, one theory is that oxyhemoglobin causes the production of superoxide radicals that lead to a decrease in nitric oxide production in endothelial cells. This decrease in nitric oxide increases protein kinase C and intracellular calcium, resulting in myofilament activation and vasospasm. Other theories involve prostaglandins and lipid peroxidases. There may also be a genetic predisposition to development of vasopasm. Preliminary studies suggest that patients with a certain polymorphism of haptoglobin ($\alpha_1\alpha_1$) may be protected against vasospasm compared to patients with haptoglobin $\alpha_2\alpha_2$, which is less effective at neutralizing free radical formation by free hemoglobin.

Borosody M, Burke A, Caplin W, et al. Haptoglobin and the development of cerebral vasospasm after subarachnoid hemorrhage. *Neurology.* 2006;66:634–640.

Vollrath AM, Weir BKA, Macdonald RL, et al. Intracellular mechanisms involved in the responses of cerebrovascular smooth-muscle cells to hemoglobin. *J Neurosurg.* 1994;80:261–268.

D.5. What are pathophysiologic changes seen in cerebral vasospasm?

Structurally, leukocytes, red blood cells, and macrophages are seen in arterial walls. Inflammatory mediators, such as eicosanoids, interleukin 1, and immune complexes, are increased. Eventually, the vessel wall thickens, and smooth muscle proliferation and collagen deposition accompany degenerative changes in the tunica intima and media.

Functionally, carbon dioxide reactivity is impaired, and autoregulation is often impaired, perhaps correlating to the degree of delayed cerebral ischemia. CBF in some areas appears to be pressure dependent, hence the reasoning behind hypertensive therapy.

Weyer GW, Nolan CP, Macdonald RL. Evidence-based cerebral vasospasm management. *Neurosurg Focus.* 2006;21:E8.

D.6. How is the diagnosis of cerebral vasospasm made?

The clinical diagnosis of cerebral vasospasm is made when the patient experiences an altered level of consciousness (drowsiness, disorientation) or a new focal neurologic deficit. These may be accompanied by increasing headache, meningismus, and fever. Vasospasm is rare in the first 3 days following SAH. It reaches peak incidence at 3 to 10 days and usually resolves by 10 to 14 days after SAH. In this patient, the new onset of hemiplegia suggests that the middle cerebral artery is involved. If vessels in the posterior fossa are involved, respiratory and hemodynamic abnormalities may develop.

The differential diagnosis includes rebleeding, hydrocephalus, seizure, hyponatremia, and drug effects. Transcranial Doppler, CBF, velocity greater than 120 cm per second in association with a new focal neurologic deficit are usually sufficient to make the diagnosis of cerebral vasospasm; however, a change in transcranial Doppler values over time may be more useful than an absolute value. CBF velocity greater than 200 cm per second is associated with a high risk of cerebral infarct, whereas a velocity less than 100 cm per second indicates that cerebral vasospasm is unlikely. Recent evidence shows that transcranial Doppler had only 63% sensitivity in identifying delayed cerebral ischemia, with a positive predictive value of only 22% in grade II and III patients.

Angiographic cerebral vasospasm can be found in 60% of patients following SAH, but only 50% of these patients will develop clinical focal neurologic deficits.

Cotrell JE, Young WL, eds. *Cottrell and Young's Neuroanesthesia.* 5th ed. Philadelphia: Mosby Elsevier; 2010:218–246.

McGrath BJ, Guy J, Borel CO, et al. Perioperative management of aneurysmal subarachnoid hemorrhage. Part 2. Postoperative management. *Anesth Analg.* 1995;81:1295–1302.

D.7. What steps can be taken to prevent cerebral vasospasm?

Calcium channel blockers are standard prophylactic therapy to prevent vasospasm. The mechanism is unknown, but presumably calcium channel blockers aid in maintaining cellular integrity by preventing calcium entry into ischemic cells. Nimodipine, taken orally, improves neurologic outcome. Patients given nimodipine have no change in overall incidence of vasospasm, but they have a lower incidence of severe narrowing. In addition, although no improvement is found in mortality, there is improvement in outcome for survivors. Intravenous nimodipine is not available in the United States.

Nicardipine, an intravenous agent, showed a lower incidence of vasospasm but no improvement in outcome versus a placebo group; both groups received hypertensive hypervolemic hemodilution therapy. The main complication of calcium channel blocker therapy is hypotension (0% to 8%), which may make this therapy difficult to achieve.

Other steps to limit cerebral vasospasm include the removal of subarachnoid blood as quickly as possible, instillation of thrombolytic agents (e.g., tissue plasminogen activator), and use of pharmacologic agents to reduce inflammatory response (high-dose glucocorticoids, ibuprofen). In Europe and Japan, protease inhibitors have been used in the treatment of vasospasm.

Weyer GW, Nolan CP, Macdonald RL. Evidence-based cerebral vasospasm management. *Neurosurg Focus.* 2006;21:E8.

D.8. What treatments can be undertaken once a diagnosis of cerebral vasospasm is made?

Treatment for cerebral vasospasm is multifactorial and includes continuation of prophylactic measures. Hypertensive hypervolemic hemodilution therapy is a plan to augment CBF past the stenotic areas. It begins with hypervolemic hypertension, with intravascular volume expansion with crystalloid or colloid to increase cardiac output. Some recommended target values are CVP of 10 to 12 mm Hg, pulmonary artery occlusion pressure of 15 to 18 mm Hg, cardiac index of 3.0 to 3.5 L/min/m^2, and hematocrit of 30% to 35%. Various blood pressure targets have been reported, but a reasonable plan is systolic blood pressure 160 to 200 mm Hg if the aneurysm is clipped and 120 to 150 mm Hg if unclipped. Vasoactive infusions are added if hypervolemia alone is inadequate. End points of therapy are resolution of neurologic deficits or occurrence of complications of therapy, such as pulmonary edema (26%), myocardial ischemia, and rebleeding or rupture of a secondary aneurysm. A pulmonary artery catheter is often indicated.

Fluid used for hypertensive hypervolemic hemodilution should be isotonic and have enough sodium to avoid hyponatremia. Vasopressin, fludrocortisone, or hydrocortisone may be administered to counteract excessive sodium and fluid loss.

Other treatments for vasospasm, including intra-arterial verapamil, papaverine or nitroprusside infusions, or angioplasty, are now more commonly used as an adjunct to hypertensive hypervolemic hemodilution therapy.

In spite of all attempted therapy, the outcome in patients with significant vasospasm is often poor. Most medications investigated to ameliorate the devastating consequences of vasospasm have had limited efficacy. Nimodipine, a calcium channel antagonist, has been found to have some efficacy in treating vasospasm and

improving outcome. A recent target of pharmacologic therapy has been endothelin, a potent long-lasting vasoconstrictor. An endothelin receptor antagonist is now in clinical trials.

Hoh BH, Ogilvy CS. Endovascular treatment of cerebral vasospasm: transluminal balloon angioplasty, intra-arterial papaverine, and intra-arterial nicardipine. *Neurosurg Clin N Am*. 2005;16:501–516.

Loch Macdonald R, Kassell NF, Mayer S, et al. Clazosentan to overcome neurological ischemia and infarction occurring after subarachnoid hemorrhage (CONSCIOUS-1): randomized, double-blind, placebo-controlled phase 2 dose-finding trial. *Stroke*. 2008;39:3015–3021.

Rinkel GJ, Feigin VL, Algra A, et al. Calcium antagonists for aneurismal subarachnoid hemorrhage. *Cochrane Database Syst Rev*. 2005;CD000277.

D.9. What are other neurologic complications following SAH and aneurysm clipping?

Hydrocephalus, manifesting with a gradual decrease in level of consciousness, occurs in 25% of patients surviving SAH. Diagnosis is confirmed by CT scan. Treatment is by ventricular drainage.

Seizures, which occur in 13% of patients with SAH, may herald rebleeding or vasospasm. Seizures cause an increase in MAP, CBF, ICP, and lactate production, predisposing to rebleeding in those patients with unclipped aneurysms, and cerebral ischemia in those patients with vasospasm. Most patients receive prophylactic anticonvulsants.

Hyponatremia occurs in 10% to 34% of patients with SAH in a time course that parallels that of vasospasm. It may be due to syndrome of inappropriate antidiuretic hormone secretion, "cerebral salt wasting," or prolonged or excessive mannitol use. Cerebral salt wasting syndrome is thought to be mediated by release of atrial natriuretic factor by the hypothalamus secondary to distention of the cerebral ventricles from hydrocephalus. After SAH, patients also have elevated plasma volume. In these patients, fluid restriction is not the treatment of choice, because hypovolemia may predispose to vasospasm. Patients with brain natriuretic peptide may be treated with an isotonic or hypertonic salt-containing fluid. In addition, treatment with hydrocortisone may be considered.

Finally, patients may experience brain swelling or edema, which is treated with mannitol or dexamethasone, or both.

Cotrell JE, Young WL, eds. *Cottrell and Young's Neuroanesthesia*. 5th ed. Philadelphia: Mosby Elsevier; 2010:218–246.

Hart RG, Byer JA, Slaughter JR, et al. Occurrence and implications of seizures in subarachnoid hemorrhage due to ruptured intracranial aneurysms. *Neurosurgery*. 1982;8:417–421.

Heros RC. Acute hydrocephalus after subarachnoid hemorrhage. *Stroke*. 1989;20:715–717.

McGirt MJ, Blessing R, Ninjee SM, et al. Correlation of serum brain natriuretic peptide with hyponatremia and delayed ischemic neurologic deficits after subarachnoid hemorrhage. *Neurosurgery*. 2004;54:1369–1374.

Moro N, Katayam V, Kojima J, et al. Prophylactic management of excessive natriuresis with hydrocortisone for efficient hypervolemic therapy after subarachnoid hemorrhage. *Stroke*. 2003;34:2807–2811.

Nelson PB, Seif SM, Maroon JC, et al. Hyponatremia in intracranial disease: perhaps not the syndrome in inappropriate secretion of antidiuretic hormone (SIADH). *J Neurosurg*. 1981;55:938–941.

D.10. What other organ systems may manifest problems postoperatively in aneurysm clipping patients?

The lungs can be affected by pneumonia or neurogenic pulmonary edema, in which disruption of the pulmonary capillary membrane occurs secondary to increased sympathetic nervous system activity. Because of inactivity, patients may be predisposed to developing deep venous thrombosis and pulmonary embolism. Patients may have fever secondary to subarachnoid blood, which may make workup of postoperative infection more difficult. In addition, as in most patients with head injury, those with SAH may have increased metabolic rate.

McGrath BJ, Guy J, Borel CO, et al. Perioperative management of aneurysmal subarachnoid hemorrhage. Part 2. Postoperative management. *Anesth Analg.* 1995;81:1295–1302.

SECTION V

The Endocrine System

CHAPTER 21

Thyrotoxicosis

Dana L. Gurvitch

A 48-YEAR-OLD MAN presented with diffuse neck swelling. History of present illness was significant for dyspnea, dysphagia, weight loss, paroxysmal palpitations, and heat intolerance. His blood pressure was 160/100 mm Hg, his heart rate was 120 beats per minute, and his hematocrit level was 29%.

A. Medical Disease and Differential Diagnosis

1. What diagnosis is compatible with these symptoms?
2. Describe the synthesis, release, and peripheral conversion of thyroxine (T_4) and triiodothyronine (T_3).
3. What is the role of the hypothalamic–pituitary axis in thyroid function?
4. Describe the effects of thyroid hormone.
5. What are the causes of hyperthyroidism?
6. What are the clinical signs and symptoms of thyrotoxicosis?
7. How would you distinguish thyroid storm from thyrotoxicosis?
8. What can precipitate thyroid storm?
9. Discuss innervation of the larynx.

B. Preoperative Evaluation and Preparation

1. Are there anatomic problems associated with an enlarged thyroid gland?
2. Describe the signs and symptoms of superior vena cava syndrome.
3. How would you assess the possibility of airway obstruction?
4. Discuss the laboratory assessment of thyroid function.
5. Describe medical strategies for achieving a euthyroid state.
6. What are the benefits of adrenergic blockade?
7. When is the hyperthyroid patient ready for elective surgery?
8. How would you premedicate this patient?
9. How would you prepare the thyrotoxic patient for emergent surgery?

C. Intraoperative Management

1. How would you monitor this patient?
2. How would you induce anesthesia?
3. Is endotracheal intubation necessary for this operation? Discuss the type and length of tube you would use.
4. How would you maintain anesthesia?
5. Intraoperatively, the patient became hyperthermic and tachycardic. Discuss the differential diagnosis of malignant hyperthermia and thyroid storm. How would you intervene?
6. How would you extubate this patient?

D. Postoperative Management

1. The patient became stridorous and dyspneic in the recovery room. What is your differential diagnosis and strategy of intervention?
2. When does thyroid storm most often present?

A. Medical Disease and Differential Diagnosis

A.1. What diagnosis is compatible with these symptoms?

These signs and symptoms are classic for hyperthyroidism. Differential diagnosis includes other hypermetabolic states such as anxiety states, carcinoid, carcinoma, choriocarcinoma, chronic infection, De Quervain thyroiditis, exertional heat stroke, Jod-Basedow thyrotoxicosis, hydatidiform mole, pheochromocytoma, polyostotic fibrous dysplasia, postpartum thyroiditis, struma ovarii, teratoma ovary, thyroid adenoma, and thyrotoxicosis factitia. In addition, certain drugs such as antipsychotic agents, anticholinergic agents, inhalation, anesthetics, serotonin antagonists, sympathomimetic agents, and strychnine poisoning must be considered.

Adler SN, Gasbarra DB, Klein DA. *A Pocket Manual of Differential Diagnosis.* Philadelphia: Lippincott Williams & Wilkins; 2008:66–67.

Fauci AS, Braunwald E, Kasper DL, et al, eds. *Harrison's Principles of Internal Medicine.* 17th ed. New York: McGraw-Hill; 2008;2224–2229, 2233–2242.

Hadad E, Wehbroum AA, Ben-Abraham R. Drug induced hyperthermia and muscle rigidity: a practical approach. *Eur J Emerg Med.* 2003;10:149–154.

Rakel RE, ed. *Saunders Manual of Medical Practice.* Philadelphia: WB Saunders; 2000:638–641.

A.2. Describe the synthesis, release, and peripheral conversion of thyroxine (T_4) and triiodothyronine (T_3).

The biosynthesis of thyroid hormone is shown in Figure 21.1. The synthesis of thyroid hormone is dependent on iodine. Sufficient amounts of iodine must come from dietary intake or from the deiodination of pre-existing thyroid hormone. Iodine is actively transported into thyroid cells mediated by the Na^+/I^- symporter and concentrated in the form of iodide. Organification occurs as iodine binds to tyrosine residues of thyroglobulin, the receptor protein for iodine. Coupling of iodinated tyrosine residues results in the formation of T_3 and T_4. Once cleaved from thyroglobulin as regulated by TSH, thyroid hormone is released into the circulation. Ninety percent of the hormone secreted from the thyroid gland is T_4, whereas only 10% is T_3, the biologically active form with a much shorter half-life. However, in the peripheral tissues, most of the T_4 is converted to T_3. T_4 can also be converted to reverse T_3, an inactive metabolite. In the circulation, most of the T_4 and

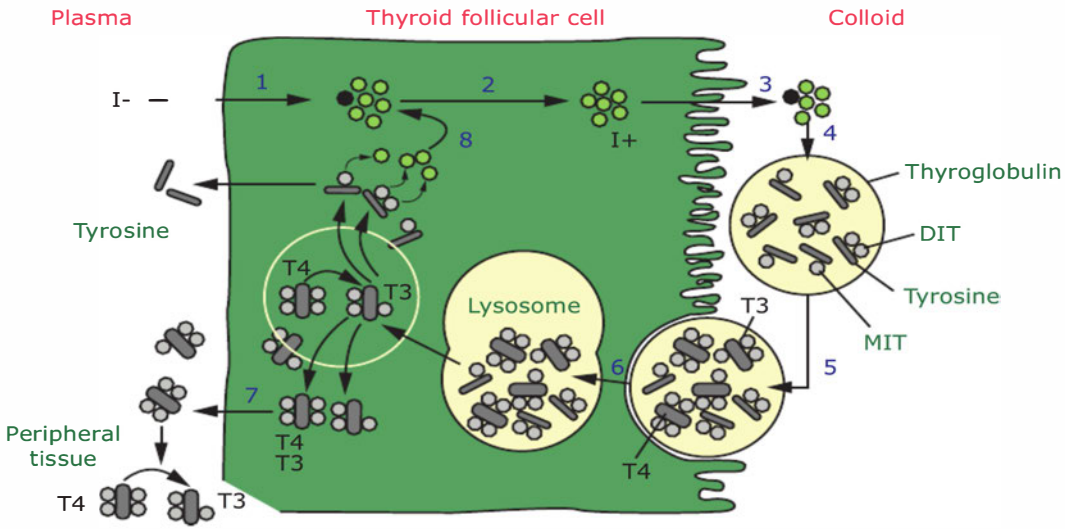

Figure 21.1 Thyroid hormone biosynthesis. Thyroid hormone synthesis includes the following steps: (*1*) iodide (I^-) trapping by the thyroid follicular cells; (*2*) diffusion of iodide to the apex of the cells; (*3*) transport of iodide into the colloid; (*4*) oxidation of inorganic iodide to iodine and incorporation of iodine into tyrosine residues within thyroglobulin molecules in the colloid; (*5*) combination of two diiodotyrosine (DIT) molecules to form tetraiodothyronine (thyroxine, T_4) or of monoiodotyrosine (MIT) with DIT to form triiodothyronine (T_3); (*6*) uptake of thyroglobulin from the colloid into the follicular cell by endocytosis, fusion of the thyroglobulin with a lysosome, and proteolysis and release of T_4, T_3, DIT, and MIT; (*7*) release of T_4 and T_3 into the circulation; and (*8*) deiodination of DIT and MIT to yield tyrosine. T_3 is also formed from monodeiodination of T_4 in the thyroid and in peripheral tissues. (Modified from Scientific American Medicine, Scientific American, New York, 1995.)

T_3 bind to plasma proteins; mainly thyronine-binding globulin. A small amount binds to albumin and transthyretin (formerly known as thyroxin-binding prealbumin), and less than 1% is unbound in the plasma. Approximately 99.8% of T_4 and 99.7% of T_3 are protein-bound. The unbound hormone is thought to be biologically available to tissues.

Fauci AS, Braunwald E, Kasper DL, et al, eds. *Harrison's Principles of Internal Medicine.* 17th ed. New York: McGraw-Hill; 2008:2224–2229, 2233–2242.

Guyton A, Hall J. *Textbook of Medical Physiology.* 12th ed. Philadelphia: WB Saunders; 2011:907–916.

Reid JR, Wheeler SF. Hyperthyroidism: diagnosis and treatment. *Am Fam Physician.* 2005;72:635–636.

A.3. What is the role of the hypothalamic–pituitary axis in thyroid function?

Hypothalamic thyroid–releasing hormone stimulates the release of thyroid-stimulating hormone (TSH) by the anterior pituitary gland; somatostatin can inhibit its release. TSH stimulates the synthesis and secretion of thyroid hormones by the thyroid gland. Within pituitary cells, T_4 is converted to T_3. The intracellular level of T_3 within pituitary cells regulates the pituitary release of TSH. Low levels of T_3 stimulate the release of TSH, whereas increased levels of thyroid hormone decrease TSH secretion.

Fauci AS, Braunwald E, Kasper DL, et al, eds. *Harrison's Principles of Internal Medicine*. 17th ed. New York: McGraw-Hill; 2008:2224–2229, 2233–2242.

Guyton A, Hall J. *Textbook of Medical Physiology*. 12th ed. Philadelphia: WB Saunders; 2011:907–916.

A.4. Describe the effects of thyroid hormone.

Thyroid hormone has effects at the cellular, organ, and systemic levels.

Cellular Effects

- Thyroid hormone regulates the nuclear transcription of messenger RNA in all cells. T_3 binds to a DNA domain named the *thyroid response element*. Once bound, T_3 initiates the transcription of an array of biochemical enzymes that regulate tissue metabolism. T_3 is also postulated to bind to mitochondrial T_3-binding proteins with resultant transcription and synthesis of cytochromes. The basal metabolic rate can increase as much as 60% to 100% when large quantities of thyroid hormones are secreted. One ubiquitous enzyme that is transcribed in response to thyroid hormone stimulation is Na,K-ATPase.
- In addition to its role in enzyme transcription, thyroid hormone regulates cellular energy use. It stimulates cellular glucose use by increasing glucose absorption from the gastrointestinal tract, glycogenolysis, gluconeogenesis, insulin secretion, and cellular uptake of glucose. Thyroid hormone increases free fatty acid availability by increasing lipid mobilization from adipocytes. Conversely, thyroid hormone decreases plasma levels of cholesterol, phospholipids, and triglycerides by increasing the rate of cholesterol secretion into the bile.

Organ Effects

- Thyroid hormone is believed to have a direct effect on the heart by increasing heart rate and contractility with resultant increases in cardiac output.
- Thyroid hormone increases oxygen consumption and carbon dioxide production with a compensatory increase in respiratory rate and tidal volume.
- Thyroid hormone increases bone formation and catabolism with resultant changes in parathyroid hormone levels.
- Normal reproductive behavior and physiology are dependent on having essentially normal levels of thyroid hormone.

Systemic Effects

- Increased cellular metabolism and production of metabolic end products result in vasodilation and enhanced tissue blood flow.

Guyton A, Hall J. *Textbook of Medical Physiology*. 12th ed. Philadelphia: WB Saunders; 2011:907–916.

Jameson J, Kasper D, Longo D, et al, eds. *Harrison's Principles of Internal Medicine*. 17th ed. New York: McGraw-Hill; 2008:2224–2229, 2233–2242.

Smallridge R. Metabolic and anatomic thyroid emergencies. *Crit Care Med*. 1992;20:276–291.

Tietgens S, Leinung M. Thyroid storm. *Med Clin North Am*. 1995;79:169–178.

A.5. What are the causes of hyperthyroidism?

Graves disease accounts for 90% of all cases of hyperthyroidism. The prevalence varies mainly on iodine intake (high iodine intake is associated with an increased

prevalence of Graves disease). Graves disease also occurs more often in women, and in persons 20 to 50 years of age. The next most common cause is thyroiditis. Less commonly, toxic multinodular goiter, toxic solitary nodule, and excessive exogenous iodide consumption (Jod-Basedow phenomenon) and side effects of certain medications can cause hyperthyroidism. Trophoblastic tumors (e.g., hydatidiform mole and choriocarcinoma) are infrequent causes of hyperthyroidism. Surreptitious overdosing (factitious thyrotoxicosis) is occasionally seen.

Kaplan MM, Meier DA, Dworkin HJ. Treatment of hyperthyroidism with radioactive iodine. *Endocrinol Metab Clin North Am.* 1998;27:205–214.

Reid JR, Wheeler SF. Hyperthyroidism: diagnosis and treatment. *Am Fam Physician.* 2005;72:623–630.

Smallridge R. Metabolic and anatomic thyroid emergencies. *Crit Care Med.* 1992;20:276–291.

A.6. What are the clinical signs and symptoms of thyrotoxicosis?

The clinical presentation depends on the severity of thyrotoxicosis, the duration of the disease, patient susceptibility to excess thyroid hormone, and the patients' age. Nonspecific constitutive signs such as sweating, heat intolerance, fatigue, polyuria, shortness of breath, weakness, and restlessness are common clinical signs and symptoms of thyrotoxicosis. Weight loss occurs despite a normal or increased appetite resulting from the increased metabolic rate. Fine tremor is a frequent finding, as is lid retraction, causing a staring appearance as a result of sympathetic overactivity.

Cardiovascular involvement is a prominent feature of thyrotoxicosis, with resulting increased cardiovascular morbidity and mortality, primarily caused by heart failure and thromboembolism. Alterations include tachyarrhythmias, increased stroke volume, increased cardiac output, increased oxygen consumption, and decreased systemic and pulmonary vascular resistance. In addition, patients demonstrate increased myocardial contractility, automaticity, and excitability. Pulse pressure can be widened with an increase in systolic blood pressure. In patients with coronary atherosclerosis, angina may be precipitated or worsened. Young adults usually tolerate hyperthyroidism without cardiovascular decompensation. However, high-output congestive heart failure can occur in older patients and in those with a previously damaged heart. Thyrotoxic patients may present with sinus tachycardia, atrial fibrillation, complete heart block, or ventricular dysrhythmias.

Hypercarbia and increased oxygen consumption resulting from the hypermetabolic state cause a compensatory increased minute ventilation with tachypnea and elevated tidal volumes. Vital capacity often decreases because of weak muscles and decreased compliance, whereas diffusing capacity remains normal. Exercise results in increased ventilation and increased oxygen uptake.

Neurologic manifestations include anxiety, agitation, tremors, insomnia, muscle weakness, and changes in cognition such as confusion and delirium. This can progress in severe cases to stupor, obtundation, and coma. Other manifestations include myopathies, periodic paralysis, seizures, chorea, and a fine resting tremor. On electroencephalogram, these patients may show an increase in fast-wave activity.

Thyrotoxicosis shortens gastrointestinal tract transit time and a secretory diarrhea may develop. Weight loss caused by increased caloric requirements is often observed. Acid secretion occasionally decreases (parietal cell antibodies in 30%), thereby potentially affecting drug absorption.

Hematologic derangements include anemia, neutropenia, and thrombocytopenia. Red blood cell mass increases because of the increased oxygen requirement.

Regarding renal involvement, tubular reabsorption and secretion are increased, leading to eventual decreased potassium excretion and increased sodium excretion.

Fauci AS, Braunwald E, Kasper DL, et al, eds. *Harrison's Principles of Internal Medicine*. 17th ed. New York: McGraw-Hill; 2008:2224–2229, 2233–2242.

Felig P, Frohman LA. The thyroid: physiology, thyrotoxicosis, hypothyroidism and the painful thyroid. In: *Endocrinology and Metabolism*. 4th ed. New York: McGraw-Hill; 2001:261–330.

Hines RL, Marschall KE. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. New York: Churchill Livingstone; 2008:380–384.

Pronovost P, Parris K. Perioperative management of thyroid disease. *Postgrad Med*. 1995;98:83–96.

Ruffi M, Cattaneo F, Tupol EJ. Thyrotoxicosis and the cardiovascular system: subtle but serious effects. *Cleve Clin J Med*. 2003;70:57–63.

A.7. How would you distinguish thyroid storm from thyrotoxicosis?

Thyrotoxicosis refers to all disorders of increased thyroid hormone concentrations. The clinical spectrum ranges from asymptomatic biochemical abnormalities to life-threatening crises with multisystem dysfunction and a high mortality rate. Thyroid storm exists when a patient's metabolic, thermoregulatory, and cardiovascular compensatory mechanisms fail. The clinical picture is characterized by hyperpyrexia (to 104° F to 106° F), tachycardia or supraventricular arrhythmias, along with congestive heart failure, central nervous system symptoms, and gastrointestinal symptoms that can include hepatic failure. Early recognition and aggressive treatment are fundamental in limiting morbidity and mortality. Criteria for the diagnosis of thyroid storm have been introduced by Burch and Wartofsky (see Table 21.1 for diagnostic criteria for thyroid storm). No laboratory test differentiates between thyroid storm and thyrotoxicosis. Thyroid function tests should be given. Nevertheless, once thyroid storm is suspected, treatment should be immediately instituted and not delayed for test results. Goals include reduction of circulating thyroid hormone levels, inhibition of the peripheral effects of circulating thyroid hormone, supportive care, and treatment of the underlying precipitating event.

Migneco A, Ojetti V, Testa A, et al. Management of thyrotoxic crisis. *Eur Rev Med Pharmacol Sci*. 2005;9:69–74.

Smallridge R. Metabolic and anatomic thyroid emergencies. *Crit Care Med*. 1992;20:276–291.

A.8. What can precipitate thyroid storm?

Thyroid storm has an abrupt onset and can be precipitated by conditions that cause a rapid rise in thyroid hormone levels such as thyroid surgery, withdrawal of antithyroid drug therapy, radioiodine therapy, iodinated contrast dyes, and vigorous thyroid manipulation. Nonthyroid illnesses such as nonthyroid surgery, infection, cerebrovascular accident, congestive heart failure, bowel infarction, pulmonary embolism, pregnancy, parturition, diabetic ketoacidosis, trauma, or administration of iodine containing materials (amiodarone) can also precipitate thyroid storm. It is the acute change of thyroid hormone levels, rather than the absolute levels that precipitates thyroid storm.

Burch H, Wartofsky L. Life threatening thyrotoxicosis. *Endocrinol Metab Clin North Am*. 1993;22:263–274.

Hines RL, Marschall KE. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. New York: Churchill Livingstone; 2008:380–384.

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Nicoloff J. Thyroid storm and myxedema coma. *Med Clin North Am*. 1985;69:1005–1012.

Table 21.1 Diagnostic Criteria for Thyroid Storm*

THERMOREGULATORY DYSFUNCTION		CARDIOVASCULAR DYSFUNCTION	
TEMPERATURE ° F (° C)	**SCORING POINTS**	**TACHYCARDIA**	**SCORING POINTS**
99–99.9 (37.2–37.7)	5	99–109	5
100–100.9 (37.8–38.2)	10	110–119	10
101–101.9 (38.3–38.8)	15	120–139	15
102–102.9 (38.3–38.8)	20	≥140	25
103–103.9 (39.3–39.9)	25	**CONGESTIVE HEART FAILURE**	
≥104.0 (>/= 40.0)	30	**Absent**	0
CENTRAL NERVOUS SYSTEM EFFECTS		**Mild** (Pedal edema)	5
Absent	0	**Moderate** (Bibasilar rales)	10
Mild (Agitation)	10	**Severe** (Pulmonary edema, Atrial fibrillation)	15
Moderate (Delirium, Psychosis, Extreme lethargy)	20	**ARTERIAL FIBRILLATION**	
Severe (Seizure, Coma)	30	**Absent**	0
GASTROINTESTINAL-HEPATIC DYSFUNCTION		**Present**	10
Absent	0	**PRECIPITATING EVENT**	
Moderate (Diarrhea, Nausea/ vomiting, Abdominal pain)	10	**Absent**	0
Severe (Unexplained jaundice)	20	**Present**	10

Scoring system: A score of 45 or greater is highly suggestive of thyroid storm; a score of 25-44 is suggestive of impending storm, and a score below 25 is unlikely to represent thyroid storm.

A.9. Discuss innervation of the larynx.

Innervation of the larynx comes from two branches of the vagus nerve: the superior laryngeal and the recurrent laryngeal nerve. The superior laryngeal nerve divides just superficial to the thyrohyoid membrane into the internal laryngeal nerve (sensory and autonomic) and external laryngeal nerve (motor). The internal laryngeal nerve pierces the thyrohyoid membrane and supplies sensory fibers to the larynx superior to the vocal cords. The external laryngeal nerve remains superficial to the thyrohyoid membrane to supply the cricothyroid muscle and a portion of the transverse arytenoid muscle. The recurrent laryngeal nerve supplies motor innervation to all of the remaining intrinsic muscles of the larynx and sensory innervation to the larynx inferior to the vocal cords.

The cricothyroid muscle is the only tensor muscle of the larynx. Bilateral recurrent laryngeal nerve injury will result in motor paralysis of all the intrinsic muscles of the larynx except the cricothyroid muscle and part of the transverse arytenoid muscle. Respiratory obstruction occurs as the vocal cords become approximated at midline. However, the cords are flaccid, not tense. The cricothyroid muscle requires resistance from the other intrinsic muscles to tense the cords. Unilateral recurrent laryngeal nerve injury results in one midline flaccid cord with the other cord being normal. Hoarseness and risk of aspiration are more problematic than respiratory obstruction.

Barash P, Cullen B, Stoelting R, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:752.

Grenvik A, Ayres S, Shoemaker W, et al, eds. *Textbook of Critical Care*. 5th ed. Philadelphia: WB Saunders; 2005:1505–1514.

Moore KL, Dalley AF. *Clinically Oriented Anatomy*. 6th ed. Baltimore: Williams & Wilkins; 2010:1042–1043.

B. Preoperative Evaluation and Preparation

B.1. Are there anatomic problems associated with an enlarged thyroid gland?

The thyroid gland incompletely encircles the trachea and esophagus. Glandular enlargement can cause tracheoesophageal compression with symptoms such as dyspnea and dysphagia. The anatomic location of the thyroid, suprasternal versus substernal, has important implications. Airway involvement can include deviation, compression, or luminal narrowing. With muscle relaxation, an enlarged substernal thyroid can cause unanticipated tracheal compression after the administration of agents that result in loss of respiratory muscle tone. Tracheal invasion or intratracheal hemorrhage can occur with thyroid carcinomas.

The anatomic position of the superior vena cava in the thorax makes it vulnerable to compression by mediastinal masses.

Acute respiratory insufficiency secondary to bilateral vocal cord paralysis from recurrent laryngeal nerve compression has been reported in patients with intrathoracic goiter.

Fauci AS, Braunwald E, Kasper DL, et al, eds. *Harrison's Principles of Internal Medicine*. 17th ed. New York: McGraw-Hill; 2008:2224–2229, 2233–2242.

Peters K, Nance P, Wingard D. Malignant hyperthyroidism or malignant hyperthermia. *Anesth Analg*. 1981;60:613–615.

Smallridge R. Metabolic and anatomic thyroid emergencies. *Crit Care Med*. 1992;20:276–291.

Steenerson R, Barton R. Mediastinal goiter and superior vena cava syndrome. *Laryngoscope*. 1978;88:1688–1690.

B.2. Describe the signs and symptoms of superior vena cava syndrome.

Superior vena cava syndrome is an insidious gradual compression or obstruction of the superior vena cava. The low-flow, low-pressure, thin-walled superior vena cava is susceptible to compression from expanding mediastinal masses. The low intravascular pressure also allows for the possibility of thrombus formation, such as catheter-induced thrombus. The obstruction of venous drainage from the upper thorax results in interstitial edema and retrograde collateral flow and produces face, neck, and upper extremity edema; dilation of collateral veins of the upper thorax and neck; and symptoms of headache and vertigo. Because of the predominance of right-sided thyromegaly, compression of the right innominate vein is more common. As the superior vena cava becomes obstructed, collaterals such as the azygous, internal mammary, vertebral, and lateral thoracic venous plexuses form. Venography is the "gold standard" for anatomic delineation.

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Walton A. Superior vena cava syndrome: an education sheet for patients. *Clin J Oncol Nurs*. 2005;9:479–480.

B.3. How would you assess the possibility of airway obstruction?

Chest radiograph, computed tomography, and magnetic resonance imaging of the neck are helpful in evaluating tracheal position and airway obstruction.

Pulmonary function testing is a noninvasive method used to evaluate patients with airway obstruction. Flow–volume loop analysis determines the extent and location of airway obstruction. Flow–volume loops are generated by inhaling to total lung capacity, exhaling to residual volume, and then inhaling back to total lung capacity. Differing patterns in flow–volume loops can distinguish intrathoracic versus extrathoracic airway obstructions (Fig. 21.2).

Fixed lesions of the upper airway, which include tracheal tumors, subglottic stenosis, and goiters cause flow limitation during both forced inhalation and forced exhalation, thus producing plateaus in both the inspiratory and expiratory cycle of the flow–volume loop (Fig. 21.2A).

Variable extrathoracic lesions are most often caused by vocal cord paralysis, vocal cord neoplasms, and neoplasms in the neck. The inspiratory limb of the flow–volume loop plateaus. During inhalation, the generation of negative intrathoracic pressure pulls the extrathoracic airway closed. During exhalation, airflow maintains the patency of the airway (Fig. 21.2B).

Variable intrathoracic lesions, which include endobronchial tumors, tracheal tumors, and tracheomalacia, produce plateau of the expiratory cycle only. Inhalation is unimpaired because negative intrathoracic pressure will stent the airway. During exhalation, positive intrathoracic pressure narrows the airway and results in plateau of the expiratory limb of the flow–volume loop (Fig. 21.2C). These patients will have preserved forced vital capacity but marked reductions of forced expiratory volume in 1 second.

Benumof J. *Anesthesia for Thoracic Surgery*. 2nd ed. Philadelphia: WB Saunders; 1995:536.

Lunn W, Sheller J. Flow volume loops in the evaluation of upper airway obstruction. *Otolaryngol Clin North Am*. 1995;28:721–729.

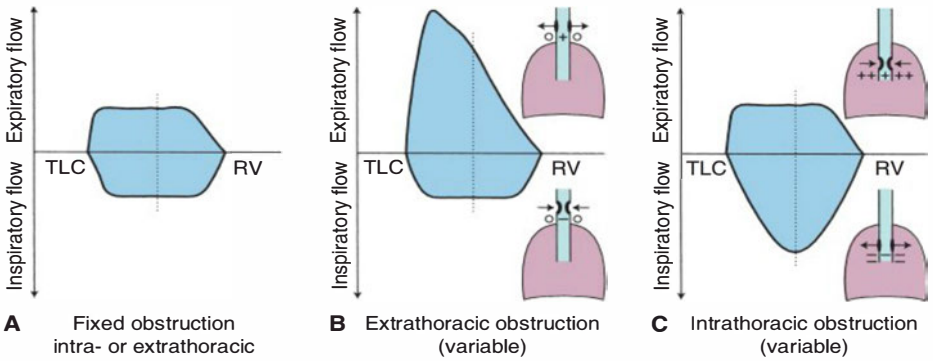

Figure 21.2 Flow–volume curves in fixed and variable obstruction. **A.** Fixed obstruction, intrathoracic or extrathoracic. **B.** Extrathoracic obstruction (variable). **C.** Intrathoracic obstruction (variable). RV, residual volume; TLC, total lung capacity. (From Benumof J. *Anesthesia for Thoracic Surgery*. 2nd ed. Philadelphia: WB Saunders; 1995:536, with permission.)

B.4. Discuss the laboratory assessment of thyroid function.

Thyroid function tests are divided into three categories:

- Direct tests of thyroid function
- Tests related to concentration and binding of thyroid hormones
- Tests of homeostatic control of thyroid function

Direct tests of thyroid function involve administration of radioactive iodine and measurement of its uptake by the thyroid. Radioactive iodine uptake is measured 24 hours after administration of the isotope. Uptake will vary inversely with the plasma iodide concentration and vary directly with thyroid function.

The patterns of thyroid function tests during assessment of thyroid function are shown in Table 21.2. Tests related to hormone concentration and binding in serum include measurements of T_4 and T_3. Radioimmunoassays of both free and total T_3 and T_4 are available. Although some centers measure the percentage of T_4 or T_3 that is dialyzable or free, most use an in vitro uptake test. Serum is enriched with labeled T_4 or labeled T_3 and is then incubated with a resin that binds free hormone. Labeled T_3 will bind to unoccupied hormone-binding sites. If these sites are already occupied by endogenous thyroid hormone, such as during hyperthyroidism, labeled T_3 will be picked up by the resin. T_3 uptake will also be elevated when thyroid-binding sites are decreased, as in low-protein states such as malnutrition, nephrotic syndrome, and liver cirrhosis. T_3 uptake is low during hypothyroidism or when thyroid-binding globulin sites are increased, such as during pregnancy, with use of oral contraceptives, and in infectious hepatitis.

Though nonspecific, serum creatinine phosphokinase (CPK), lactate dehydrogenase, and aspartate aminotransferase levels are slightly depressed in hyperthyroidism.

Tests of homeostatic control include measurement of serum TSH and thyrotropin-releasing hormone–stimulating test. TSH levels will vary inversely with thyroid hormone levels. The thyrotropin-releasing hormone stimulation test assesses the hypothalamic–pituitary–thyroid axis.

Table 21.2 Patterns of Thyroid Function Tests during Assessment of Thyroid Function

SERUM TSH	SERUM FREE T_4	SERUM T_3	ASSESSMENT
Normal hypothalamic-pituitary function			
Normal	Normal	Normal	Euthyroid
Normal	Normal or high	Normal or high	Euthyroid hyperthyroxinemia
Normal	Normal or low	Normal or low	Euthyroid hypothyroxinema
Normal	Low	Normal or high	Euthyroid: triiodothyronine therapy
Normal	Low normal or low	Normal or high	Euthyroid: thyroid extract therapy
High	Low	Normal or low	Primary hypothyroidism
High	Normal	Normal	Subclinical hypothyroidism
Low	High or normal	High	Hyperthyroidism
Low	Normal	Normal	Subclinical hyperthyroidism
Abnormal hypothalamic–pituitary function			
Normal or high	High	High	TSH-mediated hyperthyroidism
Normal or low[a]	Low or low-normal	Low or normal	Central hypothyroidism

[a] In central hypothyroidism, serum TSH may be low, normal, or slightly high.
TSH, thyroid-stimulating hormone.

de los Santos E, Mazzaferri E. Thyrotoxicosis results and risks of current therapy. *Postgrad Med.* 1990;87:277–294.

Fauci AS, Braunwald E, Kasper DL, et al, eds. *Harrison's Principles of Internal Medicine*. 17th ed. New York: McGraw-Hill; 2008:2224–2229, 2233–2242.

Smallridge RC. Metabolic and anatomic thyroid emergencies: a review. *Crit Care Med.* 1992;20:276.

Surks M, Chopra I, Mariash C, et al. American Thyroid Association guidelines for use of laboratory tests in thyroid disorders. *JAMA.* 1990;263:1529–1532.

B.5. Describe medical strategies for achieving a euthyroid state.

Medical strategy is directed at blocking the production of thyroid hormone, the release of thyroid hormone, and the adrenergic effects of excessive hormonal levels.

Initial therapy is directed at blocking thyroid hormone synthesis using antithyroid drugs such as carbimazole, propylthiouracil, and the active metabolite of the latter, methimazole. These drugs are iodinated within the thyroid gland, thus diverting iodine away from new thyroid hormone synthesis. They do not block the release of thyroid hormone and are not effective until thyroid hormone stores are depleted. Propylthiouracil also inhibits deiodination of T_4 to T_3. In addition to blocking thyroid hormone biosynthesis, these drugs lower concentrations of TSH receptor antibodies and increase activity of suppressor T cells, suggesting they have an immunosuppressive effect. Side effects of antithyroid medications include fever, urticaria, arthralgias, arthritis, leukopenia, agranulocytosis, and rarely toxic hepatitis. Glucocorticoids inhibit peripheral conversion of T_4 to T_3, and they have an additive effect when given with propylthiouracil.

After initiation of antithyroid drug therapy, iodides, such as potassium iodide, are useful to inhibit thyroid hormone synthesis and block the conversion of T_4 to T_3, thus lowering thyroid hormone levels in the blood. Onset of action occurs within 24 hours. Iodine can also be given for 8 to 10 days preoperatively to decrease the vascularity of the thyroid gland. Iodine therapy requires 2 weeks for maximal effect. A euthyroid state should be achieved with antithyroid drugs before initiating iodine therapy, otherwise the exogenous iodine can be used as substrate for the synthesis of new thyroid hormone. Exogenous iodine administration destroys functioning thyroid cells and blocks the binding of intrinsic iodine. This Wolff–Chaikoff effect lasts only a few days. Thereafter, formation of thyroid hormone resumes despite the continued high intake of iodine. Iodides are mainly useful for thyroid crisis and for emergency surgery in hyperthyroid patients. Iodine is contraindicated in children, pregnant women and women who are breast-feeding; pregnancy is reportedly safe 4 months or more after treatment.

β-antagonists are useful to block the peripheral adrenergic manifestations of hyperthyroidism. Patients become clinically euthyroid; nevertheless, without additional intervention, they will remain chemically hyperthyroid. Propranolol is the most commonly used β-adrenergic antagonist because it additionally inhibits peripheral conversion of T_4 to T_3. In thyrotoxic patients, larger doses of β-antagonists may be required because of the accelerated metabolism. Central-acting adrenergic antagonists such as reserpine or guanethidine can be used in patients who cannot take β-blockers, as can calcium channel blockade with diltiazem. Finally, cholestyramine or colestipol will bind T_4 in the gut during enterohepatic circulation and may help to bring down the T_4 level more quickly.

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Fauci AS, Braunwald E, Kasper DL, et al, eds. *Harrison's Principles of Internal Medicine*. 17th ed. New York: McGraw-Hill; 2008:2224–2229, 2233–2242.

Francis S, Greenspan, Gardner DG. *Endocrine Emergencies: Basic and Clinical Endocrinology*. 8th ed. New York: McGraw Hill; 2007:868–892.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone; 2008:380–384.

Kaplan MM, Meier DA, Dworkin HJ. Treatment of hyperthyroidism with radioactive iodine. *Endocrinol Metab Clin North Am*. 1998;27:205–214.

Smallridge R. Metabolic and anatomic thyroid emergencies. *Crit Care Med*. 1992;20:276–291.

B.6. What are the benefits of adrenergic blockade?

Catecholamines contribute to the symptoms of thyrotoxicosis. Pharmacologic agents that deplete stores or block the action of catecholamines will decrease heart rate, cardiac output, and cardiac irritability. Drugs used in the treatment of thyrotoxic symptoms include β-antagonists, combined α–β-antagonists, and central-acting agents such as reserpine and guanethidine. Side effects associated with use of these drugs include hypotension, sedation, depression, myocardial depression, bronchospasm, and diarrhea.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*, 5th ed. Philadelphia: Churchill Livingstone; 2008:380–384.

Ingbar S. Management of emergencies, thyrotoxic storm. *N Engl J Med*. 1966;274:1252–1254.

B.7. When is the hyperthyroid patient ready for elective surgery?

Emphasis should be placed on relief of symptoms. The patient should demonstrate a return of normal heart rate, pulse pressure, and sinus rhythm, as well as a resolution of recent-onset cardiac murmurs. Tremors, anxiety, palpitations, dyspnea, and heat intolerance should be relieved.

B.8. How would you premedicate this patient?

The goal of premedication of the thyrotoxic patient is to relieve anxiety and prevent the activation of the sympathetic nervous system. Benzodiazepines such as oral diazepam (5 to 10 mg) or central adrenergic blockers such as clonidine (3 to 5 μg per kg orally) are appropriate. Antimuscarinics such as atropine and scopolamine are not recommended, because they cause tachycardia and interfere with normal heat regulation.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone; 2008:380–384.

Smallridge R. Metabolic and anatomic thyroid emergencies. *Crit Care Med*. 1992;20:276–291.

B.9. How would you prepare the thyrotoxic patient for emergent surgery?

When surgery is emergent, measures should be taken to prevent thyroid storm. Reduction of the hyperadrenergic state, along with decreased conversion of T_4 to T_3, can be attempted with propranolol. Esmolol, as an alternative, may offer some advantages because of its β_1 specificity and short half-life. However, esmolol has not been shown to decrease peripheral conversion. Antithyroid drugs should be given to prevent further thyroid hormone synthesis. Either propylthiouracil, 200 to 400 mg orally every 6 hours, or methimazole, 20 to 40 mg orally every 6 hours, should be administered as

soon as possible. Methimazole in an aqueous solution, but not propylthiouracil, can be administered rectally. Propylthiouracil and glucocorticoids can also block peripheral conversion of T_4 to T_3, and together they have an additive effect. Intravenous dexamethasone 2 mg every 6 hours or hydrocortisone 40 mg every 6 hours can be administered. Saturated solution of potassium iodide 5 drops orally every 6 hours or Lugol solution 30 drops orally every 6 to 8 hours can be given to acutely inhibit release of T_4 and T_3. Parasympatholytics such as atropine and pancuronium should be avoided, because unopposed sympathetic activity may result.

Therapy should also be directed at correcting systemic decompensation. Fluids and electrolytes must be replaced. Invasive monitoring may be needed to guide the administration of inotropes and vasopressors when hypotension is unresponsive to fluids. Supportive measure with fluids, oxygen, and a cooling blanket are important. Aspirin should not be used as an antipyretic, because it displaces thyroid hormones from binding proteins and thereby raises free hormone levels. If circulatory shock is present, a direct-acting vasopressor (phenylephrine) is indicated. Unfortunately, mortality rate for thyroid storm remains at approximately 20%.

Fink NP, Abraham E, Vincent JL, et al *Textbook of Critical Care*. 5th ed. Philadelphia: WB Saunders; 2005;1510–1511.

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Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*, 5th ed. Philadelphia: Churchill Livingstone; 2008:380–384.

Tietgens S, Leinung M. Thyroid storm. *Med Clin North Am*. 1995;79:169–178.

Pronovost P, Parris K. Perioperative management of thyroid disease. *Postgrad Med*. 1995;98:83–96.

C. Intraoperative Management

C.1. How would you monitor this patient?

Once blood pressure, end-tidal carbon dioxide, pulse oximetry, electrocardiogram, and core temperature monitors are in place, the thyrotoxic patient is monitored to manage any cardiac decompensation and to recognize increased thyroid and adrenergic activity. If the patient presents to the operating room in thyroid storm, large-bore peripheral intravenous lines and an arterial line should be placed. If the patient is presently in or has a history of congestive heart failure, myocardial ischemia, renal failure, or hypotension, placement of a central venous or a pulmonary artery catheter is warranted. Invasive monitors should be placed before a skin incision is made. Once surgery has begun, access for placement of monitors will be difficult.

C.2. How would you induce anesthesia?

Induction and intubation can proceed with standard techniques if airway obstruction is not suspected. Patients with orthopnea, dyspnea, stridor, wheezing, or hoarseness require further preoperative evaluation. Preoperative studies, as described in section B.3, need to be reviewed. At a minimum, the chest radiographs must be evaluated by the anesthesiologist. Airway obstruction necessitates awake fiber-optic intubation or spontaneous inhalational induction. Inhalational induction using sevoflurane will maintain spontaneous respiration and airway patency. Isoflurane and desflurane may be too irritating to the airway for inhalational induction. Otherwise, intravenous induction with thiopental, secondary to its thiorylene nucleus and thus decrease peripheral conversion of T_4 to T_3, may have a slight advantage over other induction agents. Intubation should be attempted only after a deep plane of anesthesia is achieved. Patients with severe

obstruction may require awake intubation, which will require anesthetizing the glossopharyngeal, superior laryngeal, and recurrent laryngeal nerves. Judicious use of small amounts of amnestic or anxiolytic agents may be necessary to prevent the precipitation of thyroid storm.

A rigid bronchoscope should be available in the event of airway collapse. Emergency tracheotomies are difficult to perform because of anatomic distortion and an increase in tissue vascularity. Small reinforced endotracheal tubes should be available.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone; 2008:380–384.

C.3. Is endotracheal intubation necessary for this operation? Discuss the type and length of tube you would use.

Endotracheal intubation is necessary for thyroid surgery. If tracheal obstruction is suspected, a reinforced anode endotracheal tube should be used to prevent airway collapse. The length of the tube should be sufficient to extend beyond the thyroid gland.

C.4. How would you maintain anesthesia?

Maintenance of anesthesia should avoid sympathetic nervous system activation. Muscle relaxants are not necessary. If muscle relaxants are selected, hyperthyroid patients may have reduced requirements for the nondepolarizing muscle relaxants because they often have coexisting muscle disease (i.e., myasthenia gravis). Opioids should be given to ensure an alert patient who can maintain the airway after extubation. Treatment of hypotension with sympathomimetic drugs must take into account possible exaggerated responses. Because of the high level of circulating endogenous catecholamines, direct sympathomimetics (such as epinephrine or norepinephrine) or α-agonists (such as phenylephrine) are more appropriate than indirect sympathomimetics (such as ephedrine).

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone; 2008:380–384.

C.5. Intraoperatively, the patient became hyperthermic and tachycardic. Discuss the differential diagnosis of malignant hyperthermia and thyroid storm. How would you intervene?

Differential diagnosis includes hyperthyroid storm, malignant hyperthermia, pheochromocytoma, and carcinoid crisis. Many of the clinical manifestations of malignant hyperthermia and thyroid storm are compensatory mechanisms for hyperthermia. However, malignant hyperthermia will result in metabolic acidosis, profound hypercarbia, and muscle rigidity, which are not present during thyroid storm. Hyperthyroidism decreases the level of CPK to approximately half the normal level, whereas CPK levels are increased during malignant hyperthermia. Both disorders progress rapidly and intervention is urgent.

Once thyroid storm is suspected, treatment must start immediately. Goals of intervention include the following:

- Diagnosis and treatment of inciting event: Without treatment of the underlying cause, therapy will be less effective.

- Supportive measures: Replace fluids, glucose, and electrolytes. Reduce temperature with acetaminophen, cold lavage of body cavities, cooling blankets, ice packs, and reduction of ambient temperature. Aspirin should not be used as an antipyretic. It displaces thyroid hormones from binding proteins, thus raising free hormone levels. Inotropes, diuretics, and supplemental oxygen may be needed for acute congestive heart failure.
- Reduce secretion and production of thyroid hormones: Antithyroid drugs prevent iodide binding in the thyroid within the hour and are administered through a nasogastric tube, orally, or rectally. One hour after the administration of methimazole or propylthiouracil, iodide can be started.
- Block the metabolic effects of thyroid hormones: Metabolic manifestations can be treated with β-adrenergic blockers such as propranolol or catecholamine-depleting agents such as reserpine or guanethidine.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease.* 5th ed. Philadelphia: Churchill Livingstone; 2008:380–384.

Peters K, Nance P, Wingard D. Malignant hyperthyroidism or malignant hyperthermia. *Anesth Analg.* 1981;60:613–615.

C.6. How would you extubate this patient?

If tracheomalacia is suspected, direct visualization of airway patency is suggested. The fiber-optic bronchoscope can be used to assess for airway collapse and vocal cord movement as the endotracheal tube and bronchoscope together are slowly pulled back. If tracheal collapse is noted, the endotracheal tube and bronchoscope should be immediately readvanced. Vocal cord assessment must be done. If any question exists of the patient's ability to protect his airway, leave the endotracheal tube in place. A tracheostomy set, endotracheal tubes, and laryngoscope should be readily available at bedside.

D. Postoperative Management

D.1. The patient became stridorous and dyspneic in the recovery room. What is your differential diagnosis and strategy of intervention?

Causes of respiratory failure include hemorrhage, respiratory obstruction, recurrent laryngeal nerve palsies, tracheomalacia, pneumothorax, and hypocalcemia.

Signs of airway obstruction require emergent evaluation. Hematomas can cause compressive airway obstruction and restrict venous and lymphatic drainage of tracheal mucosa. Hematoma evacuation requires opening and drainage of incision sites. However, tracheal obstruction from mucosal edema may still persist. Patients should be intubated early before airway edema from compromised lymphatic and venous return occurs. Initially, patients should be seated upright at 45 degrees to facilitate venous drainage. Corticosteroids and racemic epinephrine via nebulization should be used to decrease laryngeal edema. If dyspnea worsens, the patient should be intubated.

Injury to bilateral recurrent laryngeal nerves results in respiratory obstruction. Patients demonstrate paramedian position of both of the true vocal cords. These patients require emergent airway intervention, including intubation or tracheotomy. Patients with unilateral recurrent laryngeal nerve paralysis present with hoarseness and minimal signs of airway obstruction.

If dissection is carried down to the mediastinum, pneumothorax must be ruled out as a cause of postoperative respiratory deterioration.

Hypocalcemia secondary to inadvertent excision of parathyroid tissue manifests within the first 3 days postoperatively. Acute airway obstruction in the immediate postoperative period is uncommon. The patient will complain of circumoral numbness and tingling of the hands and feet. If calcium is not supplemented, the patient can develop stridor and airway obstruction secondary to muscle weakness. Severe hypocalcemia can also be associated with seizures and tetany.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone; 2008:380–384.

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D.2. When does thyroid storm most often present?

Thyroid storm most often occurs 6 to 18 hours postoperatively, rather than intraoperatively. Treatment with the same regimen as outlined for emergency surgery is indicated (see section B.9). Supportive measures with fluids, oxygen, and a cooling blanket are important. Aspirin should not be used as an antipyretic, because it displaces thyroid hormones from binding proteins and thus raises free hormone levels.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone; 2008:380–384.

CHAPTER 22

Pheochromocytoma

Gregory E. Kerr

THE PATIENT IS A 39-YEAR-OLD MAN

with a history of recurrent headaches, diaphoresis, and severe hypertension for several weeks. During a physical examination, he was found to have an exceptionally high blood pressure (BP) of 230/150 mm Hg with a heart rate of 112 beats per minute. Prior to this, the patient claims to have been in good health. Further studies were obtained to evaluate the etiology of his high BP and headaches.

A. Medical Disease and Differential Diagnosis

1. What are some common problems that should be included in a differential diagnosis for hypertension?
2. What is a pheochromocytoma?
3. Trace the embryology of the adrenal gland and describe its normal anatomy.
4. What substances does the adrenal medulla excrete?
5. What are the mechanisms of action of epinephrine and norepinephrine?
6. What is the pathway for synthesis and breakdown of catecholamines?
7. What does the adrenal cortex secrete?
8. What are the metabolic actions of the glucocorticoids and the mineralocorticoids?
9. What are some clinical features associated with a pheochromocytoma?
10. In whom do we find pheochromocytoma?
11. What is the incidence of pheochromocytoma?

B. Preoperative Evaluation and Preparation

1. How can you diagnose and localize the tumor preoperatively?
2. How do you pharmacologically prepare the patient with a pheochromocytoma for surgery?
3. What other aspects of preoperative management are important?

C. Intraoperative Management

1. What drugs should be avoided during the operation?
2. How would you monitor this patient?
3. Describe acceptable options for administering anesthesia to this patient.
4. What drugs are used to control the effects of catecholamine stimulation during surgery?
5. What are some management concerns after the tumor is removed?
6. If a pheochromocytoma is found complicating pregnancy, does magnesium sulfate ($MgSo_4$) have a role in managing the hypertension?
7. What are some of the concerns with laparoscopic adrenalectomy?

D. Postoperative Management

1. What is the significance of postoperative hypotension? How is it treated?
2. What other problems can arise in the postoperative period?

A. Medical Disease and Differential Diagnosis

A.1. What are some common problems that should be included in a differential diagnosis for hypertension?

The following is a partial list of differential diagnosis of hypertension:

- *Essential hypertension*. Unknown etiology
- *Primary renal disease*. Nephritis, renal artery stenosis, and renal infarction
- *Endocrine*. Adrenocortical hyperfunction, thyroid disease, pheochromocytoma, and acromegaly
- *Hemodynamic alterations*. Decreased peripheral vascular resistance and increased intravascular volume
- *Sympathetic stimulation*. Light anesthesia, hypoxia, and hypercarbia
- *Neurogenic*. Seizure activity, elevated intracranial pressure, and denervation of the carotid sinus
- *Miscellaneous*. Malignant hyperthermia, neuroleptic malignant syndrome, carcinoid syndrome, and toxemia of pregnancy

Fauci AS, Braunwald E, Kasper DL, et al., eds. *Harrison's Principles of Internal Medicine*. 17th ed. New York: McGraw-Hill; 2008:2269.

A.2. What is a pheochromocytoma?

Pheochromocytomas are catecholamine-secreting tumors of chromaffin tissue. They are usually located in the adrenal medulla or sympathetic paraganglia, but may be found anywhere chromaffin tissue exists. These locations extend from the base of the skull to the anus. Ninety percent of pheochromocytomas are found in the adrenal medulla and 10% occur elsewhere. These are commonly called paragangliomas.

Pheochromocytomas are entities that only account for 0.1% of all cases of hypertension. They occur in only 0.005% to 0.01% of people. When unsuspected or improperly managed during surgery, the physiologic effects of the released catecholamines can be profound.

The word pheochromocytoma is derived from the Greek words for dusky, *phaios*, and color, *chroma*. In 1912, Pick noted that these tumors stained a deep rust color when treated with chromium salts.

Artusio J. Anesthesiology for pheochromocytoma. In: Malhotra V, ed. *Anesthesia for Renal and Genito-urologic Surgery*. 1st ed. New York: McGraw-Hill; 1996:80.

Hull CJ. Pheochromocytoma. *Br J Anaesth*. 1986;58:1453–1468.

Manger WM. An overview of pheochromocytoma: history, current concepts, vagaries, and diagnostic challenges. *Ann N Y Acad Sci*. 2006;1073:1–20.

Pullerits J, Ein S, Balfe JW. Anesthesia for pheochromocytoma. *Can J Anaesth*. 1988;35(5): 526–534.

Scholz T, Eisenhorfer G, Pacak K, et al. Current treatment of malignant pheochromocytoma. *J Clin Endocrinol Metab*. 2007;92(4):1217–1225.

Townsend CM, Beauchamp RD, Evers BM, et al. *Sabiston Textbook of Surgery*. 18th ed. Philadelphia: WB Saunders; 2008:1016–1021.

A.3. Trace the embryology of the adrenal gland and describe its normal anatomy.

The adrenal cortex and medulla have separate embryologic origins. The medullary portion is derived from the chromaffin ectodermal cells of the neural crest. These cells are split off very early from the sympathetic ganglion cells and migrate further ventrally, in order to lie ventrolateral to the aorta, where they form the paraganglia. Several such nodules near the cranial end of the gonads combine into a larger mass of cells lying between the dorsal aorta and the dorsomedial border of the mesonephros. Here they come into approximation with a group of mesodermal cells destined to become the adrenal cortex. These latter cells are derived principally from a narrow strip of coelomic mesothelium lying between the dorsal mesentery and the genital ridge. These cells, arising in numerous places in the suprarenal ridge, lose their connection with the mesothelium and form a complete layer of mesoderm around the ectodermal cells derived from the sympathetic ganglia. The chromaffin cells become enclosed within the cortex to form the medulla. The organs of Zuckerkandl are paraganglia around the aorta at the level of the kidney anterior to the inferior aorta. Accessory areas for the occurrence of pheochromocytoma are in the mediastinum, in the bladder, occasionally in the neck, in the sacrococcygeal region, or in the anal or vaginal areas.

Brunicardi FC, Andersen DK, Billiar TR, et al., eds. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2009:1389.

Townsend CM, Beauchamp RD, Evers BM, et al. *Sabiston Textbook of Surgery*. 18th ed. Philadelphia: WB Saunders; 2008:997–998.

A.4. What substances does the adrenal medulla excrete?

The adrenal medulla primarily secretes three substances, all of which are catecholamines. The catecholamines are epinephrine, norepinephrine, and dopamine. These three compounds are found in the chromaffin cells of the sympathetic nervous system, which includes the adrenal medulla, aberrant tissue along the sympathetic chain, and paraganglia. Both norepinephrine and dopamine are found at the endings of the postganglionic fibers of the sympathetic nervous system and in the CNS.

Brunicardi FC, Andersen DK, Billiar TR, et al., eds. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2009:1389–1392.

Townsend CM, Beauchamp RD, Evers BM, et al. *Sabiston Textbook of Surgery*. 18th ed. Philadelphia: WB Saunders; 2008:1001–1006.

A.5. What are the mechanisms of action of epinephrine and norepinephrine?

These catecholamines exert their effects by acting on β-adrenergic and α-adrenergic receptors. It is believed that the results of β-receptor stimulation are largely mediated by the stimulation of adenylate (adenylyl) cyclase, which results in the production and activation of cyclic adenosine monophosphate (cAMP). The stimulation of cAMP eventually leads to an increased inward calcium (Ca^{2+}) flux, thereby increasing cytoplasmic Ca^{2+} concentrations. The increased availability of Ca^{2+} ultimately results in enhanced actin and myosin interactions. The stimulation of α_1 receptors creates an increased inward flux of Ca^{2+} and also affects the formation of inositol triphosphate. The stimulation of α_2 receptors inhibits the action of adenylate cyclase (Fig. 22.1).

The pharmacologic response is dependent on the location of the receptors throughout the body. The distribution and density of the receptors will determine the predominant response to each catecholamine.

Brunton L, Lazo J, Parker K, eds. *Goodman and Gillman's The Pharmacologic Basis of Therapeutics*. 12th ed. New York: McGraw Hill; 2010:282–289.

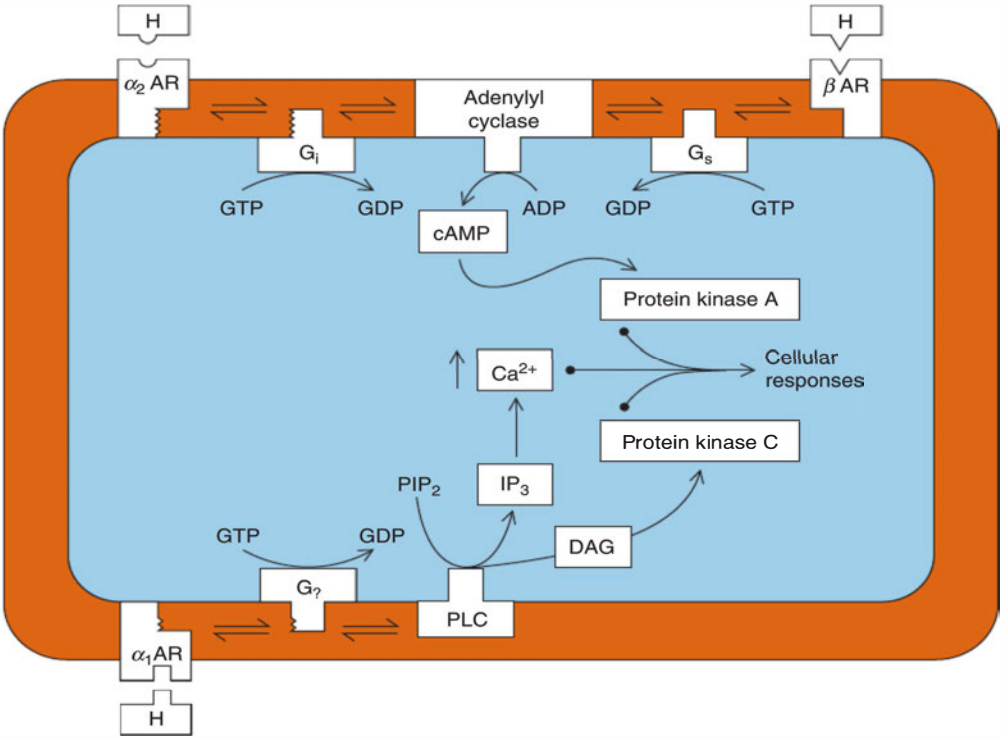

Figure 22.1 α_2-Receptor inhibition of adenylate cyclase. ADP, adenosine diphosphate; AR, adrenergic receptor; cAMP, cyclic adenosine monophosphate; Ca^{2+}, calcium; DAG, diacylglycerol; G_i, regulatory protein that, along with GTP, inhibits adenylate cyclase; G_s, regulatory protein that interacts with liganded β-adrenergic receptor to stimulate adenylate cyclase; GDP, guanosine diphosphate; GTP, guanosine triphosphate; H, neurotransmitter or hormone; IP_3, inositol triphosphate; PIP_2, phosphatidyl inositol biphosphate; PLC, phospholipase C. (Reprinted with permission from Goodman AG, Rall TW, Nies AS, et al., eds. *The Pharmacologic Basis of Therapeutics*. 8th ed. New York: MacMillan; 1993:109.)

Stoelting RK, ed. *Pharmacology and Physiology in Anesthetic Practice.* 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2005:809–812.

A.6. What is the pathway for synthesis and breakdown of catecholamines?

The synthesis of endogenous catecholamines begins with the active transport of the amino acid tyrosine from the circulation into postganglionic sympathetic nerve endings. The hydroxylation of tyrosine generally is regarded as the rate-limiting step of the pathway (Fig. 22.2). Any drug containing the 3,4-dihydroxybenzene (catecholamine) structure is rapidly inactivated by catechol-*O*-methyltransferase (COMT) or monoamine oxidase (MAO). The most important aspect of the termination of the biologic activity of these catecholamines is reuptake into the nerve endings.

Oeltmann T, Carson R, Shannon JR, et al. Assessment of O-methylated catecholamine levels in plasma and urine for diagnosis of autonomic disorders. *Autonom Neurosci Basic Clin.* 2004;116(1–2):1–10.

Schulz C, Eisenhofer G, Lehnert H. Principles of catecholamine biosynthesis, metabolism and release. *Front Horm Res.* 2004;31:1–25.

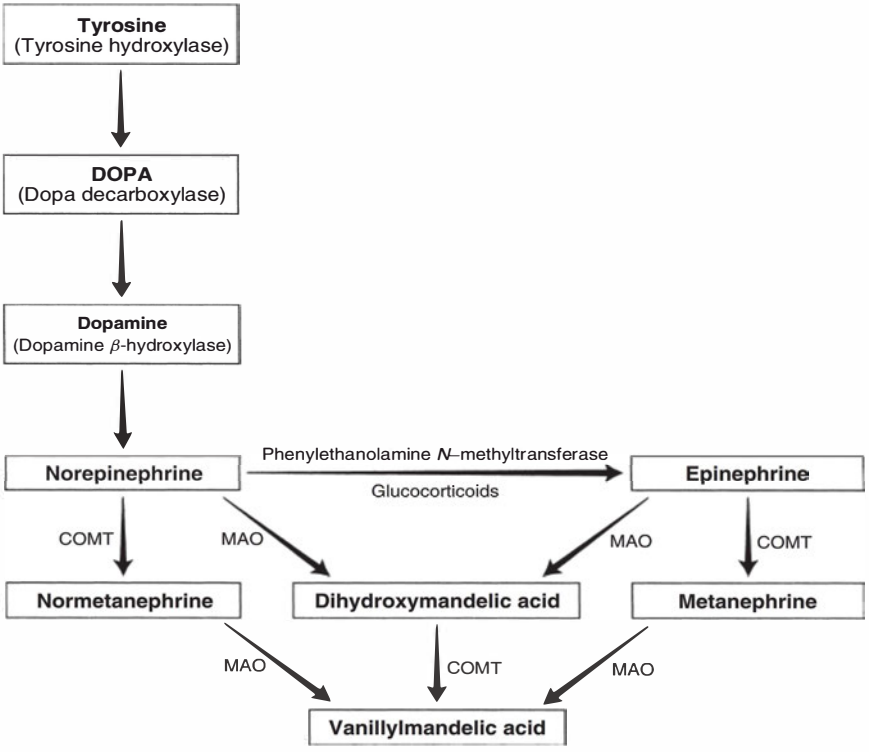

Figure 22.2 Synthesis and metabolism of endogenous catecholamine. COMT, catechol-*O*-methyltransferase; MAO, monoamine oxidase. (Reprinted with permission from Pullerits J, Ein S, Balfe JW. Anesthesia for phaeochromocytoma. *Can J Anesth.* 1988;35(5):526–534.)

A.7. What does the adrenal cortex secrete?

The adrenal cortex secretes more than 30 different corticosteroids. These can be divided into two major classes, the mineralocorticoids and the glucocorticoids. The precursor of all corticosteroids is cholesterol. Aldosterone is the most important mineralocorticoid secreted by the adrenal cortex, whereas cortisol is the most important glucocorticoid secreted. The adrenal cortex is also responsible for secreting sex steroids. Each of these substances is secreted by different zones—the mineralocorticoids are secreted by the zona glomerulosa, the glucocorticoids are secreted by the zona fasciculata, and the sex steroids (the androgens and estrogens) are secreted by the zona reticularis.

Brunton L, Lazo J, Parker K. *Goodman and Gillman's The Pharmacologic Basis of Therapeutics*. 12th ed. New York: McGraw Hill; 2010:1209–1224.

Stoelting RK, ed. *Pharmacology and Physiology in Anesthetic Practice*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2005:809–812.

A.8. What are the metabolic actions of the glucocorticoids and the mineralocorticoids?

The glucocorticoids have their predominant mechanism of action on intermediary metabolism. These effects include increased gluconeogenesis, fatty acid mobilization, protein catabolism, and anti-inflammatory effects. Cortisol may improve cardiac function by improving responsiveness of β-adrenergic receptors. Approximately 95% of the glucocorticoid activity is from the secretion of cortisol. The mineralocorticoids have their predominant action on the body minerals, sodium, and potassium. By conserving sodium ions, they sustain extracellular fluid volume. They also help maintain normal potassium plasma concentrations.

Barnes PJ. Molecular mechanisms and cellular effects of glucocorticosteroids. *Immunol Allergy Clin North Am*. 2005;25(3):451–468.

Brunton L, Lazo J, Parker K. *Goodman and Gillman's The Pharmacologic Basis of Therapeutics*. 12th ed. New York: McGraw Hill; 2010:692–694, 1209–1224.

Czock D, Keller F, Rasche FM, et al. Pharmacokinetics and pharmacodynamics of systemically administered glucocorticoids. *Clin Pharmacokinet*. 2005;44(1):61–98.

A.9. What are some clinical features associated with a pheochromocytoma?

The classic triad is severe headache, diaphoresis, and palpitations. One or more of the following often signal the presence of a pheochromocytoma: sudden severe headaches, perspiration, weight loss, paroxysmal hypertension, pallor, palpitations, diabetes-like syndrome with elevated fasting blood sugar, nausea, vomiting, fever, encephalopathy, anxiety, myocardial infarction, stroke, or acute renal failure. Although hypertension can be paroxysmal, 65% of adults demonstrate sustained hypertension. The aforementioned symptoms are usually paroxysmal in nature. These "attacks" may last from a few moments to hours.

A pressor response to particular drugs suggests the presence of this tumor. These drugs include histamine, glucagon, droperidol, tyramine, metoclopramide, cytotoxic drugs, saralasin, tricyclic antidepressants, and phenothiazines.

Artusio J. Anesthesiology for pheochromocytoma. In: Malhotra V, ed. *Anesthesia for Renal and Genito-urologic Surgery*. 1st ed. New York: McGraw-Hill; 1996:80.

Townsend CM, Beauchamp RD, Evers BM, et al. *Sabiston Textbook of Surgery*. 18th ed. Philadelphia: WB Saunders; 2008:1016–1021.

Manger WM. An overview of pheochromocytoma: history, current concepts, vagaries, and diagnostic challenges. *Ann N Y Acad Sci*. 2006;1073:1–20.

Table 22.1 Multiple Endocrine Adenomatosis

Type IIa (Sipple syndrome)	Parathyroid adenoma/hyperplasia
	Medullary carcinoma of thyroid
	Pheochromocytoma
Type IIb	Medullary carcinoma of the thyroid
	Mucosal adenomas
	Marfanoid appearance
	Pheochromocytoma
von Hippel-Landau syndrome	Hemangioblastoma of the retina, cerebellum, or other parts of the CNS, pheochromocytoma
Neurofibromatosis	Neurofibromas, café-au-lait spots, axillary or inguinal freckling, optic nerve glioma, pheochromocytoma

A.10. In whom do we find pheochromocytoma?

Pheochromocytomas occur in both sexes with peak incidence in the third to fifth decades of life. Approximately 5% of cases of pheochromocytomas are inherited as an autosomal dominant trait either alone or as part of the neoplastic syndrome, multiple endocrine adenomatosis (Table 22.1).

Artusio JF Jr. Anesthesia for Pheochromocytoma. In: Malhotra V, ed. *Anesthesia for Renal and Genito-urologic Surgery*. New York: McGraw-Hill; 1996:80.

Pullerits J, Ein S, Balfe JW. Anesthesia for pheochromocytoma. *Can J Anaesth.* 1988; 35(5):526–534.

Widimsky J Jr. Recent advances in the diagnosis and treatment of pheochromocytoma. *Kidney Blood Press Res.* 2006;29(5):321–326.

Young WF Jr. Clinical practice. The incidentally discovered adrenal mass. N Engl J Med. 2007;356(6):601–610.

A.11. What is the incidence of pheochromocytoma?

It is estimated that one to eight cases of pheochromocytoma occur per million persons annually. It seems that the incidence increases with advancing age. It also appears that there is a genetic predisposition with 10% to 20% of diagnosed patients with the disease having had a family history.

Manger WM. An overview of pheochromocytoma: history, current concepts, vagaries, and diagnostic challenges. *Ann N Y Acad Sci.* 2006;1073:1–20.

B. Preoperative Evaluation and Preparation

B.1. How can you diagnose and localize the tumor preoperatively?

The laboratory tests for pheochromocytoma are shown in Table 22.2. The biochemical diagnosis is based on the fact that pheochromocytomas release an excessive amount of catecholamines and metabolites. Urinary specimens that can be measured include urinary norepinephrine, epinephrine, dopamine, total metanephrines,

Table 22.2 Laboratory Tests for Pheochromocytoma

DIAGNOSTIC TEST	NORMAL VALUES	PHEOCHROMOCYTOMA
Blood		
Plasma catecholamines	<1,000 pg/mL	>2,000 pg/mL
Urine (24-hr collection)		
Catecholamines	<125 μg	>1,200 μg
Norepinephrine	<100 μg	Increased
Epinephrine	<1 μg	Increased
Metanephrines	<1.6 mg	>2.5 mg
Vanillylmandelic acid	<8 mg	>10 mg
Confirmation if test results are equivocal		
Clonidine suppression of norepinephrine secretion	Suppressed in essential hypertensive patients	Not suppressed
Localization of tumor		
Magnetic resonance imaging		
Computed tomography		
Scintigraphy with metaiodobenzyl guanidine (MIBG)		
Selective adrenal venous catheterization and sampling		

From Artusio J. Anesthesiology for pheochromocytoma. In: Malhotra V, ed. *Anesthesia for Renal and Genito-urologic Surgery.* New York: McGraw-Hill; 1996:84, with permission.

and vanillylmandelic acid (VMA), which are collected during a 24-hour period. The total metanephrines have given the highest true-positive results, approximately 98% to 99%.

In theory, the hydroxy-methoxy-mandelic acid (often misnamed VMA) level should be the most reliable laboratory test because it is the final common product of both catecholamine metabolic pathways. In practice, however, the intermediate metanephrines have proved to be better discriminators of pheochromocytomas. VMA is often used as an initial "case-finding" test because it has "acceptable" specificity and sensitivity and is relatively inexpensive.

Historically, 24-hour urine tests were generally considered superior to plasma tests in the diagnosis of pheochromocytomas because the tumor secretes catecholamines only intermittently and the catecholamines have a short half-life. These combined factors could result in relatively normal plasma catecholamine levels in the presence of an active tumor. Some authors have demonstrated that plasma-free metanephrines constitute the best test for excluding or confirming the presence of pheochromocytomas and should be the test of first choice for diagnosis of the tumor. Chromaginin A, a monomeric acidic protein found in the adrenal medulla, is secreted along with the catecholamines. It has been reported to have a sensitivity of 83% and a specificity of 96%. Measuring its plasma level may be useful along with the plasma levels of the catecholamines in making a diagnosis. High-pressure liquid chromatographic and radioenzyme methods for measuring levels in the plasma have also been known to improve diagnostic accuracy.

The clonidine-suppression test (which is still occasionally used) may be helpful in distinguishing the patient with a pheochromocytoma whose hypersecretion of

norepinephrine does not respond to the drug from the patient without the tumor whose high basal plasma concentration is decreased to normal by the drug.

Computed tomography (CT) with or without iodine131 (^{131}I)–labeled metaiodobenzylguanidine (MIBG) is extremely accurate in diagnosing and localizing the tumor. Use of arteriography, once popular, should be performed cautiously because dye can stimulate catecholamine release. CT scanning and magnetic resonance imaging (MRI) scanning are excellent imaging techniques that visualize normal adrenal glands when the diagnosis is equivocal. CT scanning has a sensitivity of 98%, whereas MRI is greater than 99%. For extra-adrenal locations and in pregnant patients, MRI scanning may be a more desirable choice. MIBG also has been useful in localizing extra-adrenal tumors as well as recurrent pheochromocytomas. MIBG has a specificity of greater than 95%, but a sensitivity of only 77%.

Artusio JF Jr. Anesthesiology for pheochromocytoma. In: Malhotra V, ed. *Anesthesia for Renal and Genito-urologic Surgery*. New York: McGraw-Hill; 1996:84.

Brunicardi FC, Andersen DK, Billiar TR, et al., eds. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2009:1399–1340.

Hull CJ. Phaeochromocytoma. *Br J Anaesth*. 1986;58:1453–1468.

Lenders J, Pacak K, Walther MM, et al. Biochemical diagnosis of pheochromocytomas. *JAMA*. 2002;287(11):1427–1434.

Widimsky J Jr. Recent advances in the diagnosis and treatment of pheochromocytoma. *Kidney Blood Press Res*. 2006;29(5):321–326.

Witteles BA, Kaplan EL, Roizen MF. Sensitivity of diagnosis and localization tests for pheochromocytoma in clinical practice. *Arch Intern Med*. 2000;160:2521–2524.

B.2. How do you pharmacologically prepare the patient with a pheochromocytoma for surgery?

The major goal is to partially block the responses to catecholamines and to avoid the pressor effects of the catecholamines. Although surgery remains the only definitive therapy, the above goals must be obtained as soon as the diagnosis is made by using pharmacologic methods.

Administration of α-adrenergic blockers has been the cornerstone of management. The most commonly used agents have been phenoxybenzamine (POB) (Dibenzyline 10 to 20 mg, three to four times per day orally); prazosin (2 to 5 mg two times per day orally); and phentolamine as a constant infusion. POB has been most widely used because of its relatively long duration of action and ease of administration. It irreversibly alkylates α_1-adrenergic receptors on vascular smooth muscle, thereby making them nonfunctional. It may cause postural hypotension and reflex tachycardia. These may be avoided with the careful administration of fluid volume as well as β-blockers. Be sure not to start β-blockade until the α-blockers have been started, otherwise congestive heart failure may be precipitated. Many feel that β-blockers should be used only when tachycardia or arrhythmias exist.

Prazosin has been used but does not seem to adequately prevent perioperative hypertensive episodes. Prazosin as well as $MgSO_4$, β-blockers, angiotensin-converting enzyme inhibitors, and calcium channel blockers have been used in combination with POB to attain hemodynamic stability.

α-Methyl-paratyrosine inhibits tyrosine hydroxylase. It may be given orally, gradually increasing the dose from 0.5 g per day to 4 g per day. This may decrease the catecholamine synthesis by 40% to 80%. It is very effective, but may cause diarrhea, sedative fatigue, anxiety, or agitated depression or tumors.

A study from the Cleveland Clinic suggests that preoperative use of α-blocking agents may not necessarily decrease the incidence of intraoperative hypertension or tachycardia. In fact, patients who did not receive preoperative POB had a few advan-

tages. Eighty percent of these patients did not require vasopressors in the postanesthesia care unit, although the rest did so for a very short period of time. Similarly, 79% of patients received no vasodilators in the postanesthesia care unit. There was no difference in intensive care unit length of stay between those patients who received preoperative POB/prazosin versus those who did not.

It is possible that advances in anesthetic and monitoring techniques as well as the availability of fast-acting drugs capable of correcting sudden changes in hemodynamics will allow operating on select patients without use of preoperative α-blockers. However, most physicians prefer to use α-blockers to obtund the intraoperative hypertensive responses.

Artusio JF Jr. Anesthesiology for pheochromocytoma. In: Malhotra V, ed. *Anesthesia for Renal and Genito-urologic Surgery*. New York: McGraw-Hill; 1996:80.

Boutros AR, Bravo EL, Zanettin G, et al. Perioperative management of 63 patients with pheochromocytoma. *Cleve Clin J Med*. 1990;57(7):613–617.

Connery LE, Coursin DB. Assessment and therapy of selected endocrine disorders. *Anesthesiol Clin North America*. 2004;22(1):93–123.

Prys-Roberts C, Farndon JR. Efficacy and safety of doxazosin for perioperative management of patients with pheochromocytoma. *World J Surg*. 2002;26(8):1037–1042.

B.3. What other aspects of preoperative management are important?

The circulating blood volume is decreased in many patients with pheochromocytomas. Therefore, many clinicians support the idea of administering volume (frequently blood) before surgery while patients receive α-blockade. One must be very careful with patients who have decreased myocardial function to avoid congestive heart failure. Many other clinicians feel volume loading is not necessary. They feel that if the patient has been on α-blockers for 2 weeks or more, then the volume has been restored.

Sedation for the preoperative period is considered by many clinicians to be important before surgery. Sedation may obviate the need to use high doses of antihypertensive agents before surgery.

Artusio JF Jr. Anesthesiology for pheochromocytoma. In: Malhotra V, ed. *Anesthesia for Renal and Genito-urologic Surgery*. New York: McGraw-Hill; 1996:80.

Connery LE, Coursin DB. Assessment and therapy of selected endocrine disorders. *Anesthesiol Clin North America*. 2004;22(1):93–123.

Prys-Roberts C, Farndon JR. Efficacy and safety of doxazosin for perioperative management of patients with pheochromocytoma. *World J Surg*. 2002;26(8):1037–1042.

C. Intraoperative Management

C.1. What drugs should be avoided during the operation?

As there are many agents to choose from, but many whose use is controversial, the controversial agents should be avoided (Table 22.3). This appears to be secondary to the inhibition of catecholamine reuptake. Atropine exacerbates the chronic effects of epinephrine by vagal inhibition. All drugs that release histamine (e.g., morphine, curare, atracurium) might be avoided because histamine has been known to provoke pheochromocytomas. Agents that cause an indirect increase in catecholamine levels (e.g., pancuronium, ketamine, ephedrine) should be avoided. It should be noted, however, that morphine, curare, atracurium, and pancuronium all have been used with clinical reports documenting their safe use.

Table 22.3	Suggested Drugs to Avoid in Patients with Pheochromocytoma
	Droperidol
	Morphine
	Atracurium
	Pancuronium
	Ketamine
	Ephedrine
	Halothane
	Cocaine
	Metoclopramide
	Curare

Artusio JF Jr. Anesthesiology for pheochromocytoma. In: Malhotra V, ed. *Anesthesia for Renal and Genito-urologic Surgery*. New York: McGraw-Hill; 1996:84.

Connery LE, Coursin DB. Assessment and therapy of selected endocrine disorders. *Anesthesiol Clin North America*. 2004;22(1):93–123.

Kinney MA, Narr BJ, Warner MA. Perioperative management of pheochromocytoma. *J Cardiothorac Vasc Anesth*. 2002;16(3):359–369.

Myklejord DJ. Undiagnosed pheochromocytoma: the anesthesiologist nightmare. *Clin Med Res*. 2004;2(1):59–62.

C.2. How would you monitor this patient?

Monitoring in these patients generally includes an electrocardiogram with a V_5 lead, core temperature, pulse oximetry, intra-arterial BP monitoring along with central venous pressure monitoring, and a urinary catheter. For patients with known or suspected myocardial dysfunction, a pulmonary artery catheter should be considered. One also may want to consider noninvasive techniques for assessing cardiac function.

In recent years, most of the pheochromocytomas are excised laparoscopically with minimal volume shifts and blood loss, thereby eliminating the need for central venous pressure monitoring.

Kinney MA, Narr BJ, Warner MA. Perioperative management of pheochromocytoma. *J Cardiothorac Vasc Anesth*. 2002;16(3):359–369.

C.3. Describe acceptable options for administering anesthesia to this patient.

Either general anesthesia, regional anesthesia, or a combination of the two are considered acceptable. For all techniques, it is important to avoid wide swings in BP.

For general anesthesia, induction with thiopental has been most commonly used, but induction with propofol has recently been reported to be a safe technique. One can lessen the response to intubation by administering 1.5 μg per kg lidocaine intravenously 2 minutes before laryngoscopy. Other measures to attenuate hemodynamic responses to intubation are described in Chapter 10, sections C.5 and C.6. General anesthesia may be maintained with isoflurane, sevoflurane, or desflurane, although

desflurane may be associated with occasional tachycardia. Clinicians also seem to like the concomitant use of narcotics. Some authors advocate the avoidance of halothane because of its ability to increase the incidence of arrhythmias.

Kinney MA, Narr BJ, Warner MA. Perioperative management of pheochromocytoma. *J Cardiothorac Vasc Anesth.* 2002;16(3):359–369.

Whalley DG, Berrigan MJ. Anesthesia for radical prostatectomy, cystectomy, nephrectomy, pheochromocytoma, and laparoscopic procedures. *Anesthesiol Clin North America.* 2000;18(4):899–917.

C.4. What drugs are used to control the effects of catecholamine stimulation during surgery?

Drugs used to control intraoperative hypertension are listed in Table 22.4.

Phentolamine, a short-acting α-blocking agent, can be given as a continuous infusion to control BP. Phentolamine along with isoflurane may maintain an appropriate BP. Many clinicians are becoming more comfortable with nicardipine as a way to control elevated BP.

$MgSO_4$ has been used in selected cases as an adjunct vasodilator. β-blockers are helpful during the preoperative period to control BP as well as heart rate and possible arrhythmias. Lidocaine also should be considered for the control of arrhythmias.

Diamond JA. Pheochromocytoma in a symptomatic patient with severe hypertension upon anesthesia induction. *Am J Hypertens.* 2001;14(7 pt 1):729–730.

Kinney MA, Narr BJ, Warner MA. Perioperative management of pheochromocytoma. *J Cardiothorac Vasc Anesth.* 2002;16(3):359–369.

Minami T, Adachi T, Fukuda K. An effective use of magnesium sulfate for intraoperative management of laparoscopic adrenalectomy for pheochromocytoma in a pediatric patient. *Anesth Analg.* 2002;95(5):1243–1244.

Poopalalingam R, Chin EY. Rapid preparation of a patient with pheochromocytoma with labetolol and magnesium sulfate. *Can J Anaesth.* 2001;48(9):876–880.

Table 22.4 Intravenous Drugs to Control Intraoperative Hypertension

DRUG	DOSE
Diltiazem	Load with 5- to 10-mg boluses and infuse at 0.25–0.5 μg/kg/min
Esmolol	5- to 10-mg boluses or infusion
Hydralazine	5- to 10-mg boluses every 30 min
Labetalol	10-mg boluses to total 150 mg
Magnesium sulfate	2-g boluses; be cautious in patients with renal failure and neuromuscular blockade
Nitroprusside	Infuse initially with 0.5–1.5 μg/kg/min to maximum of 8 μg/kg/min over 1–3 hr
Nicardipine	Infuse initially at 5 mg/hr; may alter rate by 2.5 mg/hr every 15 min; to maximum of 15 mg/hr
Phentolamine	1–5 mg every 5 min or infuse initially with 1 mg/min
Propanolol	1-mg boluses to total 10 mg

C.5. What are some management concerns after the tumor is removed?

It is important to be aware of the fact that BP may decrease very quickly after the blood supply of the tumor is interrupted. The BP may be maintained by administering norepinephrine as well as by administering fluids. Blood should be administered if the blood loss is substantial.

Kinney MA, Narr BJ, Warner MA. Perioperative management of pheochromocytoma. *J Cardiothorac Vasc Anesth.* 2002;16(3):359–369.

Pullerits J, Ein S, Balfe JW. Anesthesia for phaeochromocytoma. *Can J Anaesth.* 1988;35:526–534.

C.6. If a pheochromocytoma is found complicating pregnancy, does $MgSO_4$ have a role in managing the hypertension?

Reports indicate that $MgSO_4$ can be used in conjunction with several potent inhalation anesthetics to control BP. Hypomagnesemia may be present in the pregnant patient and should be corrected preoperatively. Where an adequate level of magnesium can be achieved, its use may be ideal as an adjunct to anesthetic management because it has been shown that the use of magnesium to control BP is not deleterious to the fetus.

Bullough A, Karadia S, Watters M. Phaeochromocytoma: an unusual cause of hypertension in pregnancy. *Anaesthesia.* 2001;56(1):43–46.

Grodski S, Jung C, Kertes P, et al. Phaeochromocytoma in pregnancy. *Int Med J.* 2006;36(9):604–606.

James MF, Cronje L. Pheochromocytoma crisis: the use of magnesium sulfate. *Anesth Analg.* 2004;99(3):680–686.

Widimsky J Jr. Recent advances in the diagnosis and treatment of pheochromocytoma. *Kidney Blood Press Res.* 2006;29(5):321–326.

C.7. What are some of the concerns with laparoscopic adrenalectomy?

Due to the advancement of imaging techniques, such as CT, ^{131}I MIBG scintigraphy, MRI, and positron emission tomography, localization of the tumor has become fairly accurate. These techniques allow for the selective surgical approach seen in laparoscopic surgery. Therefore, it is important to understand the issues associated with this form of adrenalectomy.

Creation of the pneumoperitoneum and, not surprisingly, manipulation of the tumor has been associated with an elevation in catecholamine and vasopressin levels in patients undergoing laparoscopic adrenalectomies. With this elevation in the catecholamine levels, there is an associated increase in cardiac output and BP. Insufflation of CO_2 into the peritoneum causes hypercarbia that can in turn increase sympathetic tone. Studies show that intraoperative hemodynamic values during laparoscopic surgery are in fact comparable to those of traditional surgery. Decreased blood loss, decreased postoperative pain, and the quicker postoperative recovery in patients who have undergone laparoscopic surgery make it the technique of choice.

Gumbs AA, Gagner M. Laparoscopic adrenalectomy. *Best Pract Res Clin Endocrinol Metab.* 2006;20(3):483–499.

Joris JL, Hamoir EE, Hartstein GM, et al. Hemodynamic changes and catecholamine release during laparoscopic adrenalectomy for pheochromocytoma. *Anesth Analg.* 1999;88:16–21.

Lombardi CP, Raffaelli M, De Crea C, et al. Role of laparoscopy in the management of adrenal malignancies. *J Surg Oncol*. 2006;94(2):128–131.

Sprung J, O'Hara JF Jr, Gill IS, et al. Anesthetic aspects of laparoscopic and open adrenalectomy for pheochromocytoma. *Urology*. 2000;55 (3):339–343.

Wilhelm SM, Prinz RA, Barbu AM, et al. Analysis of large versus small pheochromocytomas: operative approaches and patient outcomes. *Surgery*. 2006;140(4):553–559.

D. Postoperative Management

D.1. What is the significance of postoperative hypotension? How is it treated?

Postoperative hypotension is often due to hypovolemia, residual effects of phenoxybenzamine because it has a long half-life—and due to the downregulation of receptors in patients with long-standing exposure to high levels of catecholamines. Postadrenalectomy hypotension should be treated with volume administration and, if needed, norepinephrine. The presence of alpha blockade and the downregulation of receptors may require higher than usual concentrations of norepinephrine to obtain desired response. Vasopressin has been used rarely by some to treat catecholamine-resistant hypotension. Be cognizant of the fact that persistent hypotension may be secondary to bleeding.

Artusio JF Jr. Anesthesiology for pheochromocytoma. In: Malhotra V, ed. *Anesthesia for Renal and Genito-urologic Surgery*. New York: McGraw-Hill; 1996:84.

Malhotra SK, Ramprabu K, Dutta A, et al. An unusual cause of respiratory distress and hypotension following removal of a pheochromocytoma. *Can J Anaesth*. 2002;49(10):1099–1100.

Tan SG, Koay CK, Chan ST. The use of vasopressin to treat catecholamine-resistant hypotension after phaeochromocytoma removal. *Anaesth Intensive Care*. 2002;30(4):477–480.

D.2. What other problems can arise in the postoperative period?

For the first 48 hours after surgery, these patients may be very somnolent. This is possibly due to the sudden removal of activating catecholamines. Frequently, this results in decreased narcotic requirements.

Be aware that these patients also are prone to significant hypoglycemia, which alone can make a patient somnolent. In more severe cases, hypoglycemia may cause loss of consciousness and respiratory arrest. The hypoglycemia may result from decrease in epinephrine levels (especially if it is an epinephrine-secreting tumor as 10% of these tend to be) or from an increase in plasma insulin level. Neoglycogenesis and glycogenolysis, which had sustained the high blood sugar, are no longer present. Therefore, one should consider switching to a glucose-containing intravenous fluid after removal of the tumor and monitor the glucose levels very closely for at least 24 hours in the postoperative period.

Persistent hypertension after removal of a pheochromocytoma occasionally signifies that a residual pheochromocytoma tumor is present. Be aware that plasma catecholamine levels (norepinephrine) may not decrease to normal levels for many days after removal of the tumor.

Davies MJ, McGlade DP, Banting SW. A comparison of open and laparoscopic approaches to adrenalectomy in patients with phaeochromocytoma. *Anaesth Intensive Care*. 2004;32(2):224–229.

Wilhelm SM, Prinz RA, Barbu AM, et al. Analysis of large versus small pheochromocytomas: operative approaches and patient outcomes. *Surgery*. 2006;140(4):553–559; discussion 559–560.

CHAPTER 23

Diabetes Mellitus

MARK E. NUNNALLY AND VINOD MALHOTRA

A 59-YEAR-OLD WOMAN

presents for hysterectomy for cervical cancer. She is obese (body mass index 32 kg per m^2) and has had diabetes mellitus (DM) type 2, hypertension, and dyslipidemia for 20 years. She takes enalapril, metoprolol, atorvastatin, metformin, acarbose, and recently started taking insulin glargine, 20 units subcutaneously, daily for refractory hyperglycemia. She measures her serum glucose intermittently at home. Values are generally 150 to 220 mg per dL. She experiences an early and prolonged sense of fullness after meals and an unpleasant sour taste at night two or three times per week. Laboratory values are notable for a serum creatinine of 2.2 mg per dL and a serum glucose of 206 mg per dL. She has not taken any medications today and has had nothing to eat since midnight.

A. Medical Disease and Differential Diagnosis

1. What is the epidemiology of DM in the general population?
2. What are the factors in the etiology of DM?
3. How do you classify DM?
4. What are the complications of DM?
5. How would you treat the different forms of this illness?
6. How do you adequately monitor control of the disease?
7. What are some of the factors that alter insulin requirements?
8. What are the principles of management of diabetic ketoacidosis (DKA)?
9. What is a hyperglycemic hyperosmolar state?

B. Preoperative Evaluation and Preparation

1. How would you evaluate this patient?
2. How would the stiff joint syndrome affect her airway management?
3. What are the signs and implications of autonomic neuropathy in the diabetic patient?

4. How would you prepare this patient for anesthesia and surgery?
5. For elective surgery, how do you manage the insulin and glucose requirements on the day of surgery?
6. How would you premedicate this patient?

C. Intraoperative Management

1. What are the effects of anesthesia and surgery on insulin and glucose metabolism?
2. What anesthetic techniques would you employ?
3. How would you monitor this patient?
4. How would you treat hyperglycemia intraoperatively?
5. How would you recognize and treat hypoglycemic shock intraoperatively?

D. Postoperative Management

1. How would you control diabetes in this patient postoperatively?
2. Does diabetes increase perioperative risk?
3. What are the common postoperative complications you expect in a diabetic patient?
4. Is it necessary to achieve tight perioperative control of glucose?

A. Medical Disease and Differential Diagnosis

A.1. What is the epidemiology of DM in the general population?

DM, literally "sweet urine," is a group of metabolic disorders defined by elevated serum glucose. Data from the National Health and Nutrition Examination Survey from 1999 to 2002 suggest a prevalence of DM in the adult population of 9.3%, with more than a quarter of those undiagnosed. For patients 65 years or older, the prevalence is 21.6%.

A majority of patients with diabetes (approximately 90%) have type 2 diabetes (DM2); a minority (approximately 10%) have type 1 (DM1). Finally, 1% to 14% of pregnant women develop gestational diabetes. DM1 and DM2 are very different diseases. In DM1, exogenous insulin is essential for cellular metabolism. Untreated, DM1 is a wasting disease associated with ketoacidosis and severe cumulative organ failure. DM2 is a metabolic disorder associated with resistance to insulin effects. Because of the presence of circulating insulin, ketoacidosis is rare in DM2. Nevertheless, hyperglycemic hyperosmolar state is a risk in the inadequately treated patient.

Cowie CC, Rust KF, Byrd-Holt DD, et al. Prevalence of diabetes and impaired fasting glucose in adults in the U.S. population: National Health and Nutrition Examination Survey 1999–2002. *Diabetes Care.* 2006;29:1263–1268.

McDonald M, Hertz RP, Unger AN, et al. Prevalence, awareness, and management of hypertension, dyslipidemia, and diabetes among United States adults aged 65 and older. *J Gerontol A Biol Sci Med Sci.* 2009;64:256–263.

Hillier TA, Vesco KK, Pedula KL, et al. Screening for gestational diabetes mellitus: a systematic review for the U.S. Preventive Services Task Force. *Ann Intern Med.* 2008;148:766–775.

A.2. What are the factors in the etiology of DM?

Because hyperglycemia defines DM, it is too easy to focus on elevations in serum glucose, ignoring other effects. Lipid and protein metabolism are deranged in both

varieties of DM. Tissue growth, signaling, and function are likewise impaired. Simple control of blood sugar may not adequately treat the complex hormonal and metabolic derangements of DM. Inflammation and immune dysfunction are also components of the disease.

In DM1, the immune system destroys insulin-secreting pancreatic beta cells. The diagnosis of DM1 is frequently made in childhood. DM2 manifests in a variety of processes that decrease the hypoglycemic effects of insulin. Among the processes are obesity and endocrine and inflammatory conditions. In both cases, genetic association is incomplete and there is association with other diseases, including autoimmune disorders, hypertension, and dyslipidemias. Gestational diabetes reflects insulin resistance exacerbated by the effects of pregnancy. It likely signals patients who are at risk for developing DM2.

Cowie CC, Rust KF, Byrd-Holt DD, et al. Prevalence of diabetes and impaired fasting glucose in adults in the U.S. population: National Health and Nutrition Examination Survey 1999–2002. *Diabetes Care*. 2006;29:1263–1268.

McDonald M, Hertz RP, Unger AN, et al. Prevalence, awareness, and management of hypertension, dyslipidemia, and diabetes among United States adults aged 65 and older. *J Gerontol A Biol Sci Med Sci*. 2009;64:256–263.

A.3. How do you classify DM?

Table 23.1. lists the criteria for the diagnosis of DM1, DM2, and gestational diabetes. Fasting hyperglycemia is a useful means to confirm metabolic derangement, but random hyperglycemia, classic symptoms (such as polyuria and polydipsia), or the inability to manage a glucose load are sufficient to make the diagnosis. Ketoacidosis and the need for insulin reflect DM1, whereas obesity, gradual onset (usually at an older age), and hyperosmolality without ketosis suggest DM2. Gestational diabetes resembles DM2 only in the setting of pregnancy.

Therapy for DM varies by type. Insulin is essential in DM1. In DM2 and gestational diabetes, diet, exercise, and drugs that modify insulin secretion or sensitivity can help correct hyperglycemia, although exogenous insulin may be necessary.

Cowie CC, Rust KF, Byrd-Holt DD, et al. Prevalence of diabetes and impaired fasting glucose in adults in the U.S. population: National Health and Nutrition Examination survey 1999–2002. *Diabetes Care*. 2006;29:1263–1268.

McDonald M, Hertz RP, Unger AN, et al. Prevalence, awareness, and management of hypertension, dyslipidemia, and diabetes among United States adults aged 65 and older. *J Gerontol A Biol Sci Med Sci*. 2009;64:256–263.

Table 23.1 American Diabetes Association Diagnostic Criteria for Diabetes Mellitus

1.	Symptoms of diabetes plus random plasma glucose level >200 mg/dL (11.1 mmol/L)
2.	Hemoglobin $A_1C \geq 6.5\%$
3.	Fasting plasma glucose level ≥126 mg/dL (7.0 mmoL/L)
4.	Two-hour plasma glucose level ≥200 mg/dL (11.1 mmol/L) during oral glucose tolerance test

American Diabetes Association. Diagnosis and Classification of Diabetes Mellitus. [Miscellaneous Article]. *Diabetes Care*. 33 (20100100)(Supplement 1):S62, January 2010.

A.4. What are the complications of DM?

Acute complications include DKA and hyperglycemic hyperosmolar state. Both are associated with severe systemic illness and a high mortality and will be discussed separately. Hypoglycemia is a serious risk of several diabetes therapies.

Chronically, DM affects virtually every organ system. Of most concern to the anesthetist are macrovascular disease, including accelerated atherosclerosis, and microvascular nephropathy, neuropathy, and cardiomyopathy. Tissues fail from a combination of advanced glycation end products, inflammation, connective tissue proliferation, and impaired perfusion. Renal failure, neuropathy, and accelerated coronary, cerebral, and peripheral vascular disease are common. Autonomic neuropathy and the stiff joint syndrome are both factors for preoperative evaluation (see later discussion). Hypertension frequently accompanies DM, exacerbating organ failure. Impaired immune function predisposes to infection. Hypercoagulability exacerbates macrovascular disease. Dyslipidemias accelerate atherosclerotic lesions and may directly contribute to metabolic toxicities.

Cumulatively, the systemic lesions caused or exacerbated by DM reduce life expectancy. When diagnosed before the age of 35, DM causes an estimated mean of 25.9 years of lost life. Because complications present and worsen with time, this effect decreases. About 50% of mortality in diabetic patients comes from cardiovascular disease.

Although it would be helpful to stratify diabetic patients according to their risk for complications, the complexity of the disease and its management has made stratification difficult. The assumption is that a diabetic is at high risk for coronary and other macrovascular disease, congestive heart failure, and renal insufficiency.

Ford ES, Zhao G, Li C. Pre-diabetes and the risk for cardiovascular disease. *J Am Coll Cardiol*. 2010;55:1310–1317.

Stolar M. Glycemic Control and complications in type 2 diabetes mellitus. *Am J Med*. 2010;123:S3–S11.

A.5. How would you treat the different forms of this illness?

Diabetes care is different in chronic and acute settings. It is essential to differentiate between the agents used chronically and during acute perioperative stress.

Care of DM1 requires exogenous insulin. Figure 23.1 illustrates the pharmacodynamics of several insulin preparations. A combination of a short- and a long-acting insulin preparation can help achieve the goals of resting and postprandial glycemic control. In contrast, DM2 responds to insulin, oral insulin secretagogues, insulin sensitizers, glucose uptake inhibitors, gastrointestinal hormones, weight loss, dietary management, and exercise. Table 23.2 lists the major classes of drugs available for the treatment of DM, mechanisms of action, pharmacokinetics and particular concerns for the anesthetist.

Certain medications have side effects that deserve consideration. Biguanides, such as metformin, increase peripheral glucose uptake but also predispose patients to greater production of lactic acid and acidosis. The significance of this finding is not clear, but many recommend discontinuing these drugs perioperatively because hypoperfusion states are possible during surgery. Because of its long half-life, metformin may take up to 72 hours to clear from the bloodstream, so discontinuation on the day of surgery does not minimize the risk of acidosis. Thiazolidinediones have been associated with hepatic injury and congestive heart failure. Exanatide is associated with reports of kidney dysfunction. Sulfonylureas, pramlintide, and sitagliptin may be associated with hypoglycemia.

For these reasons, as well as unreliable pharmacokinetics, the best option for acute treatment of all types of diabetic hyperglycemia is insulin. Although subcutaneous

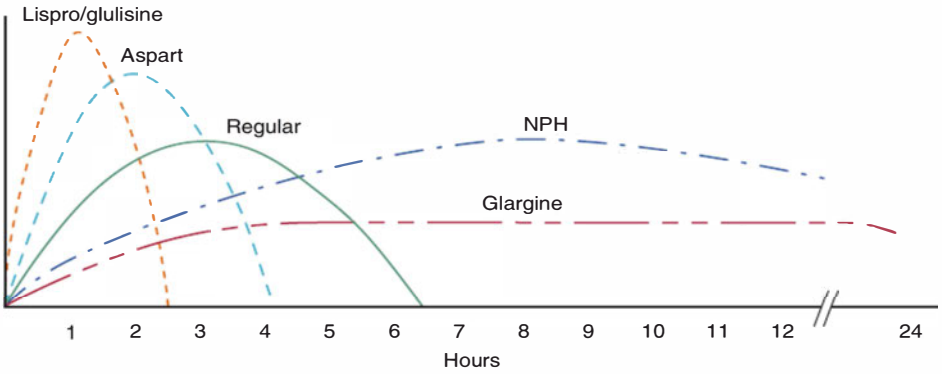

Figure 23.1 Onset and duration of action graphic for common subcutaneous insulin preparations. Regular insulin given intravenously fits the best profile for a titratable drug in the operating room, as onset peak and offset all occur within an hour.

dosing is often used in the hospital setting, intravenous insulin best meets the profile of an ideal titratable agent. It has a short time to onset (10 to 15 minutes), peak effect (less than 30 minutes), and duration of action (45 minutes). Frequent glucose monitoring is essential to titrate the therapy.

Although serum glucose or other markers of chronic hyperglycemia, such as hemoglobin (Hgb) A_1C are currently standard end points for therapy, other factors such as serum lipid and blood pressure management may be just as important. Anesthesiologists should inquire about agents treating these conditions during preoperative evaluation.

Bagry HS, Raghavendran S, Carli F. Metabolic syndrome and insulin resistance. *Anesthesiology*. 2008;108:506–523.

Chen D, Lee SL, Peterfreund RA. New therapeutic agents for diabetes mellitus: implications for anesthetic management. *Anesth Analg*. 2009;108:1803–1810.

A.6. How do you adequately monitor control of the disease?

Self-monitoring of blood glucose is possible in all forms of diabetes, usually by using finger-stick blood samples and portable monitors. This method is the established standard of care in DM1 for carefully titrated control to prevent hypoglycemia and ketoacidosis. Many advocate self-monitoring for patients with DM2, especially if they take insulin, but compliance varies and self-monitoring may not be beneficial in all patients. Hgb A_1C, the product of hemoglobin exposure to hyperglycemic conditions, is a marker of long-term glycemic control. It may help identify subgroups of patients for whom the risk for complications is higher and can be a marker of disease control. The relationship between levels of glycemic control and Hgb A_1C is not linear, however, and the single laboratory value does not completely reveal the glycemic profile over time. Patients with DM should have blood pressure and serum lipid profiles monitored, because these factors increase the risk for complications.

In the operating room, glucose can be measured with samples from a pinprick or venous or arterial line. Samples from a venous or arterial line offer greater reliability during low perfusion. If insulin is being used, monitoring is recommended every hour.

Table 23.2 Common Therapies for Type 2 Diabetes (DM2)[a]

DRUG NAME/CLASS	MECHANISM	ROUTE	ONSET	DURATION	IMPORTANT CONSIDERATIONS
1st Generation Sulfonylureas	↑ Beta cell insulin secretion	PO			Hypoglycemia risk
Tolbutamide			1 hr	12 hr	
Acetohexamide			3 hr	24 hr	
Tolazamide			4 hr	16 hr	
Chlorpropamide			2 hr	24 hr	
2nd Generation Sulfonylureas	↑ Beta cell insulin secretion	PO			Hypoglycemia risk
Glyburide (Micronase)			30 min	24 hr	
Glipizide IR (Glucotrol)			30 min	24 hr	
Glipizide ER (Glucotrol XL)			2–4 hr	24 hr	
Glimepiride (Amaryl)			2–3 hr	24 hr	
Biguanides	↑ Peripheral glucose uptake in response to insulin	PO			Lactic acidosis risk may extend up to 72 hr after administration
Metformin (Glucophage)			1–3 hr	17 hr	
α-Glucosidase inhibitors	↓ Digestive carbohydrate breakdown	PO			No known adverse effects
Acarbose (Precose)			2 hr	NA	
Miglitol (Glyset)			2–3 hr	NA	
Thiazolidinediones (PPAR-γ mediators)	↑ Peripheral glucose uptake	PO			Risk for hepatic injury, fluid retention; ongoing concerns about myocardial ischemia
Pioglitazone (Actos)			hours	$T_{1/2}$ 3–7 hr	
Rosiglitazone (Avandia)			hours	$T_{1/2}$ 3–4 hr	

Glinides	↑ Beta cell insulin secretion	PO			Hypoglycemia risk
Repaglinide (Prandin)			15–60 min	4–6 hr	
Nateglinide (Starlix)			20 min	$T_{1/2}$ 1.5 hr	
Incretin-mimetics	↑ Insulin, ↓ glucagon, hepatic glucose production, gastric emptying, and appetite	SC			Observational data associate with renal failure
Exenatide (Byetta)			10 min	6–8 hr	
Liraglutide (Victoza)			minutes	$T_{1/2}$ 13 hr	
DPP-IV Inhibitors	Inhibits incretin breakdown	PO			May have effects on immune function
Sitagliptin (Januvia)			hours	days	
Saxagliptin (Onglyza)			hours	24 hr	
Amylin Analogues	↑ Satiety, ↓ glucagon, and appetite	SC			No confirmed hypoglycemia risk
Pramlintide (Symlin)			minutes	hours	

[a]Onset and duration data are approximate only and subject to variability.
PPAR, peroxisome proliferator-activated receptor; PO, per os (by mouth); SC, subcutaneous.

Kolb H, Kempf K, Martin S, et al. On what evidence-base do we recommend self-monitoring of blood glucose? *Diabetes Res and Clin Pract.* 2010;87:150–156.

Moitra V, Sladen RN. Monitoring endocrine function. *Anesthesiol Clin.* 2009;27:355–364.

A.7. What are some of the factors that alter insulin requirements?

Insulin responsiveness is dynamic during stress or illness. Tissue injury, from surgery or trauma, or inflammatory states, such as infection, decrease responsiveness to insulin as part of the stress response. Under ideal circumstances, these effects are maximal 2 to 3 days after injury and resolve over the course of a week, but there is substantial variability. Besides stress, any other condition that increases counter-regulatory hormones such as glucagon, cortisol, and catecholamines decreases insulin sensitivity and increases insulin requirements. Cushing's disease and pheochromocytoma are examples of conditions that cause insulin resistance. Several medications, including corticosteroids, thyroid replacement preparations, oral contraceptives, and thiazide diuretics also increase insulin resistance. In solid organ transplant recipients, corticosteroids and the calcineurin inhibitor tacrolimus have been associated with insulin resistance or onset of diabetes. Exercise and ethanol can decrease insulin requirements.

Shah T, Kasravi A, Huang E, et al. Risk factors for development of new-onset diabetes mellitus after kidney transplantation. *Transplantation.* 2006;82:1673–1676.

Tanaka T, Nabatame H, Tanifuji Y. Insulin secretion and glucose utilization are impaired under general anesthesia with sevoflurane as well as isoflurane in a concentration-independent manner. *J Anesth.* 2005;19:277–281.

Thorell A, Nygren J, Ljungqvist O. Insulin resistance: a marker of surgical stress. *Curr Opin Clin Nutr Metab Care.* 1999;2:69–78.

A.8. What are the principles of management of diabetic ketoacidosis (DKA)?

A hyperglycemic patient should be assessed for DKA before surgery. Because DKA is associated with a higher perioperative mortality, patients should be monitored for intravascular volume and electrolyte abnormalities.

Withholding insulin contributes to DKA, as does infection or tissue injury, which exacerbates diabetes and sets off a chain of events that can result in DKA. Because of increased risk to the patient, DKA is corrected before surgery. When DKA is triggered by a surgical condition, time to correct it may be limited by the urgency of the surgery.

Patients with DKA have an anion gap metabolic acidosis in addition to hyperglycemia. Elevated serum ketone levels can help confirm the diagnosis, but urine ketones are frequently easier to assay. Commonly, a patient will be hypovolemic from polyuria and incomplete hydration, and resuscitation with isotonic fluids is appropriate. Because lactate and acetate are converted to glucose by the liver, solutions containing these fluids should be avoided in the initial resuscitation. Ketosis is corrected with insulin, which is best as an intravenous infusion. Because glucose levels frequently normalize before ketosis clears, insulin therapy is continued even after hyperglycemia corrects. Dextrose is administered simultaneously to avoid hypoglycemia. During acidemia, hyperkalemia is common from shifts in body stores. Frequently, a patient will have a net potassium deficit. Hypokalemia during correction, which can reflect a deficit of up to 10 mEq potassium per kg body mass, should be treated aggressively. Likewise, hypocalcemia and hypomagnesemia should be anticipated and treated.

Kitabchi AE, Matteri R, Murphy MB, et al. Is a priming dose of insulin necessary in a low-dose insulin protocol for the treatment of diabetic ketoacidosis? *Diabetes Care.* 2008;31:2081–2085.

Kitabchi AE, Nyenwe EA. Hyperglycemic crises in diabetes mellitus: diabetic ketoacidosis and hyperglycemic hyperosmolar state. *Endocrinol Metab Clin N Am.* 2006;35:725–751.

A.9. What is a hyperglycemic hyperosmolar state?

Any hyperglycemic patient should be evaluated for a hyperglycemic hyperosmolar state, another potentially fatal condition. The syndrome is more frequent in DM2. It includes hyperglycemia, hyperosmolarity, volume depletion, and changes in mental status. Adverse effects result from hyperosmolarity and hypovolemic shock. Glucose levels exceeding 1,000 mg per dL have been described. Mortality can be very high. Glycosuria and inadequate fluid intake contribute to the condition. Treatment consists of fluid resuscitation and intravenous insulin to correct the hyperglycemia. Sodium, potassium, calcium, and magnesium levels are evaluated and normalized.

Kitabchi AE, Nyenwe EA. Hyperglycemic crises in diabetes mellitus: diabetic ketoacidosis and hyperglycemic hyperosmolar state. *Endocrinol Metab Clin N Am.* 2006;35:725–751.

B. Preoperative Evaluation and Preparation

B.1. How would you evaluate this patient?

The goals of preoperative evaluation should be to stratify perioperative risk, ensure optimal management of concurrent illness, and screen for specific anesthetic-related problems. A diabetic patient is evaluated for cardiovascular disease, renal function, stiff joint syndrome, autonomic neuropathy, aspiration risk, and acute diabetic emergencies that can be treated.

Both DM1 and DM2 increase the risk of coronary artery disease. The 2007 American College of Cardiology and American Heart Association Guidelines on Perioperative Cardiovascular Evaluation and Care for Noncardiac Surgery recommend the use of the Revised Cardiac Risk Index. This index uses a history of diabetes, ischemic heart disease, heart failure, cerebrovascular disease, and renal insufficiency to predict perioperative cardiovascular risk. When the patient's functional capacity is low and surgical risk is intermediate to high, the guidelines recommend that the index be used to determine whether the patient needs noninvasive testing (e.g., stress testing) before surgery. With diabetes, the answer is yes if it will change perioperative management. The guidelines recommend heart rate control when any risk factors, including diabetes, are present.

Testing is most useful when it changes management. Noninvasive testing for cardiovascular disease in the diabetic patient adds little if the anesthetic plan is the same regardless of the results. For this reason, the guidelines suggest testing before intermediate risk or vascular surgery plus one or two of the listed risk factors as an alternative to surgery with heart rate control. For three or more risk factors, coupled with intermediate risk or vascular surgery, the recommendation is to consider testing if it will change management. The guidelines emphasize that the literature is inconclusive, that testing improves outcome, and that surgery-specific risks, such as hemodynamic or oxygenation perturbations, be considered when assessing the need for testing. The overall impact of diabetes is to make noninvasive testing a consideration

in all but the lowest risk surgeries when a patient has poor exercise tolerance, if the results will change management.

Optimizing the patient's medical status is a consideration for all patients, but particularly for diabetics who have many comorbidities. Optimal management of coexisting hypertension and congestive heart failure can minimize perioperative risk. The decision to proceed or delay a procedure for medical management depends on the urgency of the surgery and the potential for improving the patient's medical condition.

Diabetes is a leading cause of renal insufficiency and failure. Because this patient already has an increased serum creatinine, she should be further screened for renal insufficiency and any fluid and metabolic derangements should be corrected. A metabolic panel, including serum creatinine, blood urea nitrogen, potassium, sodium, chloride, bicarbonate, and base deficit can be useful, especially because angiotensin mediators, beta-blockers, and insulin itself can affect serum potassium levels. Joint stiffness is assessed with a comprehensive airway examination and the "prayer sign," in which a patient's hands are placed against each other at the palmar surface to see whether the fingers touch. Other considerations in the patient with diabetes include the risks of aspiration and autonomic instability. Although Hgb A_1C levels correlate with perioperative risk, the test does not add any information to the decision paradigm.

In addition to its chronic consequences, diabetes may produce a hyperglycemic hyperosmolar state and DKA. Both syndromes reflect severe metabolic abnormalities, most commonly associated with infection. Because these syndromes may manifest as the result of a surgical emergency, patients with these conditions will present for perioperative management. Ideally, metabolic derangements should be corrected before anesthetic induction, but sometimes, patients must go to surgery urgently or emergently. Anesthesia providers should be prepared for hemodynamic instability, rapid fluid infusion, electrolyte repletion, and frequent serum glucose and electrolyte monitoring. In both cases, intravenous insulin infusion is indicated, titrated to normoglycemia in hyperglycemic hyperosmolar state and the clearance of ketones in DKA. Supplemental dextrose is usually necessary to maintain insulin infusion in the latter.

Fleisher LA, Beckman JA, Brown KA, et al. ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: a report of the American College of Cardiology/American Heart Association task force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery). *J Am Coll Cardiol*. 2007;50:e159–e242.

Lee TH, Marcantonio ER, Mangione CM, et al. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. *Circulation*. 1999;100:1043–1049.

B.2. How would the stiff joint syndrome affect her airway management?

The stiff joint syndrome is thought to result from glycation of connective tissue with chronic exposure to hyperglycemia. The range of motion may be reduced in the cervical spine and temporomandibular and arytenoid joints, making endotracheal intubation difficult. As a screening tool, the prayer sign suggests the presence of joint stiffness. If the patient cannot completely oppose the palmer surface of her hands, she may also have reduced mobility in her glottic structures. Neck range of motion and oral aperture should be assessed; the prayer sign might suggest the need for a small endotracheal tube for a narrow glottis or difficult airway adjuncts.

Hogan KJ. Difficult laryngoscopy and diabetes. *Anesth Analg*. 1988;67:1162–1165.

Salzarulo HH, Taylor LA. Diabetic "stiff joint syndrome" as a cause of difficult endotracheal intubation. *Anesthesiology*. 1986;64:366–368.

B.3. What are the signs and implications of autonomic neuropathy in the diabetic patient?

Diabetic neuropathy involves both the peripheral and autonomic nervous system. In the autonomic system, gastric motility, heart rate, and vasomotor tone can be impaired. Cardiac ischemia can be asymptomatic. This patient can be at risk for pulmonary aspiration of gastric contents and/or hemodynamic instability. A history elicits early satiety, prolonged postprandial fullness, and significant reflux symptoms. Potential difficulties with mask ventilation and intubation are assessed. Heart rate variability, best seen on an electrocardiogram tracing in response to deep breathing, Valsalva maneuver, or position changes, identifies patients at risk for hemodynamic instability. Preparation is made to control hemodynamic instability, especially because this patient is taking angiotensin-converting enzyme inhibitors or angiotensin receptor blocking agents. Because of a high likelihood of hemodynamic instability, the anesthesiologist should prepare to use slow titration of anesthetic agents, frequent blood pressure monitoring, and vasoactive agents, if necessary.

Huang CJ, Kuok CH, Kuo TBJ, et al. Pre-operative measurement of heart rate variability predicts hypotension during general anesthesia. *Acta Anaesthesiol Scand.* 2006;50:542–548.

B.4. How would you prepare this patient for anesthesia and surgery?

This patient's cardiovascular risk is elevated, and insulin therapy is given for hyperglycemia. Because of her elevated serum glucose, she is asked about polyuria, a sign that she might be dehydrated from hyperglycemic diuresis. DKA is unlikely because she has DM2, but a metabolic panel is indicated to rule out electrolyte abnormalities.

If her exercise tolerance is below 4 metabolic equivalents, about the equivalent of climbing a flight of stairs or dancing, noninvasive stress testing may be considered. An ECG is indicated based on her risk factors for cardiovascular disease.

Her symptoms, consistent with gastroparesis and gastroesophageal reflux, will influence premedication and airway management. Results from a comprehensive airway examination, including assessment of neck and jaw mobility and a check for the prayer sign, affect anesthetic management decisions. A rapid-sequence intubation could minimize aspiration risk, but only if intubation is easy. If a difficult airway is suspected, awake intubation techniques should be considered.

B.5. For elective surgery, how do you manage the insulin and glucose requirements on the day of surgery?

The risk for hypoglycemia is balanced against the benefit of tight glycemic control. Anesthetized patients can have occult hypoglycemia, so serum glucose is checked frequently. Intravenous insulin is titrated for glycemic control. When administered intravenously, insulin has a fast onset and a short duration of action either as an infusion or as intermittent boluses. Subcutaneous insulin, with longer-lasting effects, is less predictable, especially during the hemodynamic changes of anesthesia and surgery. Subcutaneous insulin pumps should be turned down or off for all but the most minor procedures. Similarly, oral agents should be withheld on the day of surgery, except in very minor procedures. Ideally, metformin should be withheld for 72 hours to minimize the risk of lactic acidosis.

Initial enthusiasm for tight glycemic control in critically ill patients has given way to a much more cautious approach. Perioperatively, hyperglycemia is associated with

worsened neurologic and cardiac ischemia and poor wound healing. Even though tight control of serum glucose has been associated with better outcomes, there is risk associated with the therapy. Hypoglycemia is a serious risk with insulin; the drug has multiple other effects that remain poorly described.

Evidence is limited to support glycemic control to a "normal" range of 80 to 110 mg per dL in the operating room. Higher targets minimize hypoglycemia. Levels higher than 180 mg per dL should be avoided, in part, because of protein glycation and osmotic diuresis above this level. Targets within the range of 100 to 180 mg per dL are considered satisfactory.

Preoperative infusion of dextrose minimizes peripheral insulin resistance and reduces the risk of hypoglycemia. When it results in hyperglycemia, it increases the amount of insulin needed. Given that insulin resistance and hyperglycemia are parts of the stress response to surgery, hyperglycemia may be a sign that exogenous carbohydrate infusion is not necessary.

Coursin DB, Connery LE, Ketzler JT. Perioperative diabetic and hyperglycemic management issues. *Crit Care Med*. 2004;32:S116–S125.

Lipshutz AKM, Gropper MA. Perioperative glycemic control. *Anesthesiology* 2009;110:408–421.

B.6. How would you premedicate this patient?

Concerns with premedication include sensitivity to sedatives and aspiration risk. Pre-existing cardiovascular, cerebrovascular, and renal disease temper the aggressiveness of administration of benzodiazepines and opioids. Because of the symptoms of gastroesophageal reflux and gastroparesis, histamine blockers, liquid antacids, or metoclopramide may be given. Metoclopramide, famotidine, and a liquid antacid such as sodium citrate will minimize aspiration risk in this patient.

C. Intraoperative management

C.1. What are the effects of anesthesia and surgery on insulin and glucose metabolism?

As part of the stress response to surgery, metabolism increases and resistance develops to the hypoglycemic effects of insulin. The response includes the mobilization of protein stores (mostly muscle), more hepatic gluconeogenesis, and greater breakdown and synthesis of triglycerides. Hormones, including catecholamines, cortisol, glucagon, and even insulin, contribute to the metabolic changes. Although glucose metabolism increases, production of glucose also increases, adding to the risk of hyperglycemia. Administration of exogenous dextrose can exacerbate hyperglycemia in patients with diabetes patients.

Anesthetic techniques influence metabolism, but generally to a lesser extent than the stress from surgical injury. Techniques that mitigate stress hormones, such as neuraxial anesthesia, also may mitigate hyperglycemia. Some drugs effect regulatory hormones directly. Etomidate blocks cortisol synthesis. Benzodiazepines can decrease cortisol secretion. Halogenated agents have in vitro effects on insulin secretion. Nevertheless, none of these effects have an impact on postoperative glycemic control as much as will the surgery itself.

McAnulty GR, Robertshaw HJ, Hall GM. Anaesthetic management of patients with diabetes mellitus. *Br J Anaesth*. 2000;85:80–90.

C.2. What anesthetic techniques would you employ?

Factors other than glycemic control may influence the choice of anesthetic technique in the patient with diabetes. Regional techniques should be chosen based on provider skill, patient preferences, and postoperative pain control. Techniques that speed the time to oral intake by reducing nausea or minimizing ileus make glycemic management easier postoperatively. For this reason, antiemetics and the spare use of opioids might be beneficial. Although not a contraindication to nerve blockade, peripheral neuropathy should be documented in a preoperative neurologic examination. Nerve injury from local anesthetics or abnormalities on neurologic examination may complicate postoperative management. Infection risk in patients with diabetes may be realized because of complications of regional techniques.

Sedated or anesthetized patients cannot complain of hypoglycemia symptoms in the same way unsedated patients can. Serum glucose is monitored regularly in all but the shortest cases.

In this patient, general endotracheal anesthesia with precautions to prevent aspiration, intravenous insulin titrated to a serum glucose of less than 180 mg per dL, and frequent blood glucose monitoring is a satisfactory choice.

Ljungqvist O, Nygren J, Soop M, et al. Metabolic perioperative management: novel concepts. *Curr Opin Crit Care.* 2005;11:295–299.

McAnulty GR, Robertshaw HJ, Hall GM. Anaesthetic management of patients with diabetes mellitus. *Br J Anaesth.* 2000;85:80–90.

C.3. How would you monitor this patient?

If preoperative evaluation reveals a risk for hemodynamic instability, cardiac ischemia, or congestive heart failure, added cardiovascular monitoring should be considered, based on the nature of the procedure. Peripheral vascular disease can complicate placement of an arterial catheter, but is not a contraindication, because in patients who have cardiovascular comorbidities, the benefits of monitoring outweigh the risks.

Frequent glucose monitoring, by finger stick, or ideally, by venous or arterial sample, in cases lasting more than an hour is recommended when hypoglycemic agents are being used. Serum glucose should be measured at least every hour when giving intravenous insulin.

In this patient, pulse oximetry, continuous ECG monitoring, end-tidal carbon dioxide and gas analysis, and noninvasive blood pressure monitoring are satisfactory, if no further concerns arise from cardiovascular evaluation.

McAnulty GR, Robertshaw HJ, Hall GM. Anaesthetic management of patients with diabetes mellitus. *Br J Anaesth.* 2000;85:80–90.

C.4. How would you treat hyperglycemia intraoperatively?

The high end of a normal range for fasting serum glucose is 110 mg per dl, but hyperglycemia in inpatients may be at a higher level.

The one good agent for treating intraoperative hyperglycemia is intravenous insulin. Onset takes minutes, peak effect is achieved in 15 to 30 minutes, and duration of effect is less than an hour, facilitating titration. Insulin may be administered by continuous infusion or as intermittent boluses; the bolus consumes less lead time and eliminates the risk of pump misprogramming or malfunction. Subcutaneous insulin is less ideal for use during general anesthetics or complex procedures because

variable peripheral blood flow will alter the uptake and duration of action of insulin. Most other therapies for DM2 are not fit for intraoperative use. Oral agents cannot be easily administered, are not reliably absorbed, and have too long a duration of action to be practical perioperatively. They may be taken on the day of surgery before minor procedures. Metformin, a biguanide, increases the risk of lactic acidosis during periods of hypoperfusion. Metformin is discontinued for 3 or more days before extensive procedures when a large-volume blood loss is possible.

Smiley DD, Umpierrez GE. Perioperative glucose control in the diabetic or nondiabetic patient. *South Med J.* 2006;99:580–589.

C.5. How would you recognize and treat hypoglycemic shock intraoperatively?

Hypoglycemia can lead to tissue energy failure and has been associated with hemodynamic collapse and brain injury. Any patient receiving insulin, pramlintide, sitagliptin, or sulfonylureas is at risk for hypoglycemia. Because risk is usually known beforehand, hourly or more frequent monitoring of serum glucose should detect hypoglycemia. If glucose levels are low or decrease rapidly, the fastest treatment is a bolus of intravenous dextrose, 50% solution, administered slowly. In an emergency, one full ampule is the starting dose. In less urgent settings when the serum glucose level is low but not critical, smaller doses can be titrated to serum glucose values.

Dierdorf SF. Anesthesia for patients with diabetes mellitus. *Curr Opin Anaesthesiol.* 2002;15:351–357.

D. Postoperative Management

D.1. How would you control diabetes in this patient postoperatively?

Unless a change in disease status occurs as a consequence of surgery or preoperative care was inadequate, this patient should be transitioned back to her preoperative regimen. Before transitioning, she must recover from the stress response to the surgery. If this were a simple outpatient procedure, such as a cataract extraction, she could return home on her outpatient medication regimen. In this case, the effects of tissue injury may not peak for several days; diabetes control is thus a dynamic challenge. Regular monitoring of glucose is required (at a minimum checks should be made every 6 hours).

She is monitored for hyperglycemia, and her nutrition regimen is adjusted to serum glucose measurements. Hourly glucose measurements and glucose infusions can control hyperglycemia. Most patients can be effectively managed with subcutaneous insulin and less-frequent measurements. Insulin dose should take into account preoperative requirements, insulin resistance from the stress response, and caloric intake. Many patients receive intravenous dextrose postoperatively; if they are hyperglycemic on this regimen, dextrose is discontinued.

Oral diabetes medications can be reintroduced once the acute stress response begins to wane and the patient is cleared for a normal diet. Resumption of an oral diet can increase the risk of hyperglycemia, so ongoing monitoring is essential.

Smiley DD, Umpierrez GE. Perioperative glucose control in the diabetic or nondiabetic patient. *South Med J.* 2006;99:580–589.

D.2. Does diabetes increase perioperative risk?

Because patients with diabetes are at a greater risk for atherosclerosis, infection, autonomic and cardiovascular instability, and metabolic abnormalities than those without diabetes, perioperative risk is higher in this patient population. After surgery, the diabetic patient is monitored for hyperglycemia and hypoglycemia, ischemic complications, circulatory compromise, and wound and nosocomial infection. As a group, patients with diabetes have an increased risk of complications and poor outcomes from complications.

Lipshutz AKM, Gropper MA. Perioperative glycemic control. *Anesthesiology*. 2009;110: 408–421.

D.3. What are the common postoperative complications you expect in a diabetic patient?

Hyperglycemia and hypoglycemia, wound infections, and organ ischemia are the most common and worrisome postoperative complications in patients with diabetes. After myocardial infarction or cerebrovascular accident, hyperglycemia is associated with a worse prognosis.

Smiley DD, Umpierrez GE. Perioperative glucose control in the diabetic or nondiabetic patient. *South Med J*. 2006;99:580–589.

D.4. Is it necessary to achieve tight perioperative control of glucose?

In the critical care setting, there is evidence for improved outcomes with tight glycemic control, variably defined as serum glucose between 80 and 120 mg per dL or higher, as well as evidence of no benefit or even harm. Some advocate for tight glycemic control in cardiac and noncardiac surgery. The risk of hypoglycemia and data from more recent studies have tempered the enthusiasm for tight glycemic control.

Potential benefits from tight glycemic control include improvement in metabolic, anti-inflammatory, organ, and circulatory function. Unfortunately, there is little evidence to suggest these benefits are substantial perioperatively. Unresolved issues are the best time for tight control, the goals of therapy, the effect of nutrition, and the magnitude and factors in the potential for significant hypoglycemia. The patient is transitioned to her preoperative level of control during recovery, and severe hyperglycemia is avoided by monitoring glucose closely. Glucose levels above 180 mg per dL increase the risk of protein glycation and osmotic diuresis; targeting serum glucose below this value makes physiologic sense.

Gandhi GY, Nuttall GA, Abel MD, et al. Intensive intraoperative insulin therapy versus conventional glucose management during cardiac surgery. *Ann Intern Med*. 2007;146:233–243.

The NICE-SUGAR Study Investigators. Intensive versus conventional glucose control in critically ill patients. *N Engl J Med*. 2009;360:1283–1297.

Van den Berghe G, Wouters P, Weekers F, et al. Intensive insulin therapy in critically ill patients. *N Engl J Med*. 2001;345:1359–1367.

SECTION VI

The Genitourinary System

CHAPTER 24

Transurethral Resection of the Prostate

Jerome F. O'Hara, Jr., Mauricio Perilla, Vinod Malhotra, and Fun-Sun F. Yao

A 79-YEAR-OLD MAN

with benign prostatic hypertrophy was scheduled for transurethral resection of the prostate (TURP). His past medical history includes myocardial infarction (MI) 7 months ago requiring drug-eluting coronary stent placement and an implantable cardioverter-defibrillator (ICD) inserted for episodes of ventricular tachycardia. His current left ventricular ejection fraction is 25%. The patient is taking diuretics, a β-blocker, ticlopidine (an antiplatelet agent), aspirin, and an angiotensin-converting enzyme (ACE) inhibitor. Medical assessment advice was to continue platelet therapy for 1 year postcardiac stent.

A. Medical Disease and Differential Diagnosis

1. Are there differences in morbidity and mortality rates between TURP and suprapubic or retropubic prostatectomy?
2. What chronic medical conditions are common in patients who have undergone TURP?
3. Does a history of prior MI increase the patient's risk of perioperative reinfarction?
4. In patients with a history of recent MI, would you recommend that the surgery be postponed for a certain period? If so, why? If not, why not?

B. Preoperative Evaluation and Preparation

1. How would you evaluate the patient's cardiac condition? What additional tests would you have liked to order? Would you recommend that the patient undergo coronary angiography before surgery? Explain.
2. Are patients with a Q-wave infarction at greater risk of reinfarction than those with a non–Q-wave infarction? If so, why? If not, why not?
3. Would you discontinue any antihypertensives or any medications for angina? Why or why not?
4. For a patient with an ICD, what information should you know? What precautions should be taken?
5. What types of coronary stents are available? What is their perioperative relevance?
6. What is the conventional recommendation for antiplatelet therapy in a patient with previous percutaneous coronary intervention (PCI) undergoing noncardiac surgery?
7. What risk is associated with perioperative antiplatelet therapy?
8. How should patients with coronary stents undergoing noncardiac surgery be approached?

C. Intraoperative Management

1. What monitors would you use for this patient?
2. What anesthetic technique is preferable for patients undergoing TURP, and why?
3. Does regional anesthesia result in a lower incidence of perioperative mortality than general anesthesia? Whether yes or no, explain why or why not.
4. What intravenous fluid would you use during TURP?
5. Forty minutes after a sensory level of T-10 was established with intrathecal anesthesia, and monopolar TURP resection was initiated with the use of glycine as the bladder irrigating solution, the patient becomes agitated and complains of nausea. Further sedation along with an antiemetic are administered. However, shortly thereafter, the patient becomes very restless, blood pressure rises, and heart rate decreases. The patient becomes cyanotic and obtunded, blood pressure precipitously falls, pupils are dilated and unresponsive to light. What is the most likely cause of these signs and symptoms, and would these occur during bipolar or laser TURP resection?
6. What are the important characteristics of irrigation solutions used during TURP?
7. Why is plain distilled water rarely used for irrigation during TURP? What types of irrigation solutions are available?
8. What is the effect on body temperature of continuous bladder irrigation during TURP?
9. What is the definition of TURP syndrome? What are the signs and symptoms of the syndrome?
10. How can hyponatremia occur if the bladder irrigating fluid is not absorbed via the prostatic vessels?
11. How does the patient absorb irrigation solution during TURP? How much irrigation solution is typically absorbed?
12. How can one estimate the volume of irrigation solution absorbed during TURP?
13. What is the relation between the duration of surgery and the incidence of TURP syndrome?
14. What factors increase the incidence of TURP syndrome?

15. What is the effect on cardiopulmonary, renal, and central nervous system (CNS) functions of excessive absorption of irrigation solution during TURP?
16. What causes CNS dysfunction in patients who have undergone TURP?
17. What is the physiologic role of sodium ions in the body? What is the effect of excessive absorption of irrigation solution on serum sodium level?
18. What is the relation between serum sodium level and the incidence of neurologic symptoms in patients who have undergone TURP?
19. How does acute hyponatremia affect the cardiovascular system?
20. What prophylactic measures may reduce the incidence of TURP syndrome?
21. What therapeutic measures are recommended for patients with TURP syndrome?
22. Is normal saline administration always necessary to correct hyponatremia? Explain. What are the risks of rapidly correcting hyponatremia?
23. What are the toxic effects of glycine? Is there an antidote to glycine toxicity? What are the metabolic byproducts of glycine?
24. What are the symptoms and clinical course of TURP-induced hyperammonemia?
25. Why do some patients who have undergone TURP develop hyperammonemia and others do not? Is there a preventive treatment for hyperammonemia in these patients?
26. What are the clinical characteristics, causes, and prognosis of TURP-related blindness?
27. What gynecologic procedure has been associated with a syndrome similar to TURP syndrome?
28. What are the causes of excessive bleeding during TURP?
29. What triggers disseminated intravascular coagulopathy in patients undergoing TURP? How would you treat it?
30. What are the causes, signs, symptoms, and treatment of bladder perforation during TURP?
31. What are the causes, signs, symptoms, and preventive measures for bladder explosion during TURP?
32. What are the causes of hypotension during TURP?

D. Postoperative Management

1. What is the source of postoperative bacteremia in patients who have undergone TURP? What factors increase the incidence of bacteremia?
2. What are the signs of post-TURP septicemia? What preventive measures are generally recommended?
3. What bacteria-related cause may possibly lead to sudden postoperative shock in patients who have undergone TURP?
4. Is postoperative hypothermia a risk factor for myocardial ischemia?
5. How would you diagnose perioperative MI?

E. Comparing Monopolar, Bipolar, and Laser TURP

1. What differentiates monopolar from bipolar TURP?
2. Are decreased morbidity and mortality associated more closely with monopolar TURP than with bipolar TURP?
3. What differentiates the technologies for laser TURP?

F. Are There Preferred Anesthetic and Preferred Surgical TURP Techniques for This Patient?

A. Medical Disease and Differential Diagnosis

A.1. Are there differences in morbidity and mortality rates between TURP and suprapubic or retropubic prostatectomy?

Many urologists and prostate surgeons consider TURP to be a simpler and safer procedure than "open" prostatectomy. However, despite many improvements in anesthesia and surgery, 7% of patients who have undergone TURP sustain major complications and approximately 1% die perioperatively. On the other hand, no differences have been observed in mortality rates between patients who have undergone TURP and those who have undergone retropubic or suprapubic prostatectomy.

Malhotra V. Transurethral resection of prostate. *Anesthesiol Clin North America.* 2000;18: 883–897.

A.2. What chronic medical conditions are common in patients who have undergone TURP?

TURP patients often are elderly and suffer from cardiac, pulmonary, vascular, and endocrinologic disorders. The incidence of cardiac disease is 67%; cardiovascular disease, 50%; abnormal electrocardiogram (ECG), 77%; chronic obstructive pulmonary disease, 29%; and diabetes mellitus, 8%. Occasionally, these patients are dehydrated and depleted of essential electrolytes because of long-term diuretic therapy and restricted fluid intake.

Gravenstein D. Transurethral resection of the prostate (TURP) syndrome: a review of the pathophysiology and management. *Anesth Analg.* 1997;84:438–446.

Malhotra V. Transurethral resection of prostate. *Anesthesiol Clin North Am.* 2000;18:883–897.

A.3. Does a history of prior MI increase the patient's risk of perioperative reinfarction?

Yes, a history of prior MI or ischemic heart disease is considered an intermediate predictor of perioperative cardiac morbidity; but conditions like unstable coronary syndrome, severe angina, or recent MI indicate major clinical risks. Also see Chapter 13, Section A.1.

A.4. In patients with a history of recent MI, would you recommend that the surgery be postponed for a certain period? If so, why? If not, why not?

An acute MI (7 days or less), or a recent MI (more than 7 days but less than or equal to 1 month), is considered an event requiring evaluation to determine if there is residual myocardium at risk. The stratification is based on the presentation of the disease; patients with active ischemia are at highest risk. Therefore, it seems prudent to wait at least 6 weeks after an MI before surgery is performed, although no evidence supports this precaution. Also see Chapter 13, Secton A.6.

Fleisher LA, Beckman JA, Brown KA, et al. ACC/AHA 2007 Guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery). *Circulation.* 2007;116:e418–e499.

B. Preoperative Evaluation and Preparation

B.1. How would you evaluate the patient's cardiac condition? What additional tests would you have liked to order? Would you recommend that the patient undergo coronary angiography before surgery? Explain.

The American College of Cardiology/American Heart Association guidelines suggest a stepwise approach that takes into account the clinical markers of cardiac risk, functional capacity, and surgery risk. The patient's medical history should focus on information about previous cardiac evaluations and interventions (coronary stent and automatic implantable cardioverter-defibrillator [AICD] placement). During physical examination of all organ systems, attention should be paid to the circulatory functions, especially in the presence of active cardiac conditions such as unstable coronary syndromes, decompensated congestive heart failure (CHF), significant arrhythmias, or severe valvular disease. The functional capacity of the patient is best evaluated by the activity history. Minimally, a routine ECG and chest radiograph should be obtained. If the patient presents signs and symptoms of CHF, angina, syncope, or arrhythmia, further cardiac testing should be considered if the results would impact the patient's management. Traditional indications for coronary angiography apply regardless of future surgical interventions.

Fleisher LA, Beckman JA, Brown KA, et al. ACC/AHA 2007 Guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery). *Circulation.* 2007;116:e418–e499. doi:10.1161/CIRCULATIONAHA.107.185699

B.2. Are patients with a Q-wave infarction at greater risk of reinfarction than those with a non–Q-wave infarction? If so, why? If not, why not?

Recent studies suggest that patients who survive a non–Q-wave infarction are at greater risk of reinfarction than those who survive a Q-wave infarction.

Antman EM, Braunwald E. ST-elevation myocardial infarction; pathology, pathophysiology and clinical features. In: Zipes D, Libby P, Bonow R, et al., eds. *Braunald's Heart Disease, A Textbook of Cardiovascular Medicine.* 7th ed. Philadelphia: WB Saunders; 2005:1141–1166.

Landesberg G. Pathophysiology of perioperative myocardial infarction: facts and perspectives. *J Cardiothorac Vasc Anesth.* 2003;17:90–100.

Priebe HJ. Perioperative myocardial infarction—aetiology and prevention. *Br J Anaesth.* 2005;95:3–19.

B.3. Would you discontinue any antihypertensives or any medications for angina? Why or why not?

Antianginal agents and β-blockers should be continued until the day of the surgery to prevent rebound hypertension and tachycardia that may result from sudden withdrawal of these drugs. Patients taking ACE inhibitors or angiotensin II receptor antagonists might present intraoperative hypotension due to a decrease of intravascular volume. It has been suggested that ACE inhibitors or angiotensin II receptor antagonists be withheld on the day before surgery and readministered after adequate intravascular volume has been established in order to avoid renal dysfunction.

Fleisher LA, Beckman JA, Brown KA, et al. 2009 ACCF/AHA focused update on perioperative beta blockade incorporated into the ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines 2007. *Circulation.* 2009;120:e169–e276.

B.4. For a patient with an ICD, what information should you know? What precautions should be taken?

Patients undergoing surgery with ICD need to be evaluated by the device clinic before surgery. Recent and accurate information should be collected about the device's features, the date of insertion, and the indication for placement. On the day of surgery, the device should be assessed for settings, pace dependency, baseline rhythm and rate, tachyarrhythmia history, effect of magnet, and battery status.

In the event of potential electromagnetic interference, the antitachycardia algorithm of the ICD should be turned off and external cardioversion paddles should be placed until the device is set to its initial functions after the procedure. Also see Chapter 7, sections B and C.

Practice Advisory for the Perioperative Management of Patients with Cardiac Implantable Electronic Devices: Pace makers and Implantable Cardioverter-Defibrillators: an updated report by the American Society of Anesthesiologists task force on perioperative management of patients with cardiac implantable electronic devices. *Anesthesiology.* 2011;114:247–261.

B.5. What types of coronary stents are available? What is their perioperative relevance?

Percutaneous coronary intervention (PCI) is a common procedure in the United States. Coronary stent placement was introduced in order to reduce the risk of thrombosis, dissection, and restenosis after angioplasty. Two types of coronary stents have been used: bare metal stents (BMS) and drug-eluting stents (DES). Two types of drug-eluting stents—sirolimus and plaquitaxel-eluting stents—have been used extensively to reduce the neointimal hyperplasic reaction seen with the use of BMS, which is the main cause of restenosis. Emerging evidence suggested that DES inhibited or delayed the endothelization of coronary stent struts. Patients with DES are at risk for late thrombosis if the antiplatelet therapy is prematurely interrupted.

Grines CL, Bonow RO, Casey DE Jr., et al. Prevention of premature discontinuation of dual antiplatelet therapy in patients with coronary artery stents: a science advisory from the American Heart Association, American College of Cardiology, Society for Cardiovascular Angiography and Interventions, American College of Surgeons, and American Dental Association, with representation from the American College of Physicians. *J Am Coll Cardiol.* 2007;49:734–739.

B.6. What is the conventional recommendation for antiplatelet therapy in a patient with previous percutaneous coronary intervention (PCI) undergoing noncardiac surgery?

Therapy with thienopyridines (ticlopidine or clopidrogel) and aspirin is recommended for 2 to 4 weeks after dilatation without stenting; surgery should be

postponed for 2 to 4 weeks. After BMS, antiplatelet therapy for 4 to 6 weeks is recommended; elective surgery should be postponed for 4 to 6 weeks. After the implantation of DES, at least 12 months of antiplatelet therapy is required; elective surgery should be delayed for 12 months. In patients with an indication of PCI and a projected elective surgery within the next 12 months, a balloon angioplasty or BMS may be considered. In general, daily aspirin should be continued during the perioperative period, but in the case of TURP, the risk of bleeding complications must be balanced against the risk of stent thrombosis, MI, and cardiac death (rebound effect). It may be noted, however, that continuation of aspirin is not a contraindication to neuraxial anesthesia. For more details, see Chapter 9, section A.5 and Figures 9.1 and 9.2.

Abualsaud AO, Eisenberg MJ. Perioperative management of patients with drug-eluting stents. *J Am Coll Cardiol Interv*. 2010;3:131–142.

Fleisher LA, Beckman JA, Brown KA, et al. 2009 ACCF/AHA focused update on perioperative beta blockade incorporated into the ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2009;120:e169–e276.

Horlocker TT, Wedel DJ, Rowlingson JC, et al. Regional anesthesia in patients receiving antithrombotic or thrombolytic therapy. American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (Third Edition). *Reg Anesth and Pain Med*. 2010;35:64–101.

Popescu WM. Perioperative management of the patient with a coronary stent. *Curr Opin Anaesthesiol*. 2010;23:109–115.

B.7. What risk is associated with perioperative antiplatelet therapy?

The results of studies on the risk of surgical bleeding with aspirin are inconsistent. In Burger's review and meta-analysis (aspirin withdrawal vs. low-dose aspirin), the low-dose group's relative risk of bleeding increased by a factor of 1.5, but there was no increase in bleeding complications or in perioperative mortality, with the possible exceptions of intracranial surgery and prostatectomy. Studies with ticlopidine or clopidrogel are also contradictory. Although some data support increased risk of major perioperative bleeding with dual-antiplatelet therapy (0.4% to 1%), there is no consensus regarding withholding thienopyridines. The risk of perioperative bleeding must be balanced against protection from a coronary event.

Fleisher LA, Beckman JA, Brown KA, et al. 2009 ACCF/AHA focused update on perioperative beta blockade incorporated into the ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2009;120:e169–e276.

Howard-Alpe GM, de Bono J, Hudsmith L, et al. Coronary artery stents and non-cardiac surgery. *Br J Anaesth*. 2007;98:560–574.

B.8. How should patients with coronary stents undergoing noncardiac surgery be approached?

The preoperative evaluation of patients with coronary stents should include information regarding the date of stent placement, the coronary anatomy before the intervention, the type of coronary stent, the localization of the intervention, complications (if any) during the procedure, the residual anatomy after the intervention (e.g., possibility of incomplete

revascularization), and the antiplatelet strategy. Multidisciplinary discussions regarding how the risk of bleeding compares with the risk of coronary stent thrombosis are strongly encouraged. The most recently published *Practice Alert* indicates, "Elective surgery with a significant risk of bleeding should be postponed until the recommended course of thienopyridine therapy has been completed." For bare-metal coronary stents, postponement of 4 to 6 weeks is recommended, and for drug-eluting coronary stents, 12 months of postponement. If surgery must be performed and if thienopyridine therapy must be interrupted (surgery with high risk of perioperative bleeding), aspirin should be continued and thienopyridine should be readministered as soon as possible after the procedure. Bridge therapies have been proposed for patients who undergo surgical procedures, but this practice has not been shown to reduce the risk of thrombosis. Currently, continuing double antiplatelet therapy is recommended in patients with DES for surgery with minor or intermediate risk of perioperative bleeding. *A careful "case-by-case" consideration is advisable. Discussion between the anesthesiologist, the surgeon, and the treating cardiologist is recommended.* For more details, see Chapter 9, section A.5 and Figures 9.1 and 9.2.

Abualsaud AO, Eisenberg MJ. Perioperative management of patients with drug-eluting stents. *J Am Coll Cardiol Intv.* 2010;3:131–142.

American Society of Anesthesiologists Committee on Standards and Practice Parameters. Practice alert for the perioperative management of patients with coronary artery stents: a report by the American Society of Anesthesiologists Committee on Standards and Practice Parameters. *Anesthesiology.* 2009;110:22–23.

Newsome LT, Weller RS, Gerancher JC, et al. Coronary artery stents: II. Perioperative considerations and management. *Anesth Analg.* 2008;107:570–590.

Popescu WM. Perioperative management of the patient with a coronary stent. *Curr Opin in Anaesthesiol.* 2010;23:109–115.

C. Intraoperative Management

C.1. What monitors would you use for this patient?

The following monitors would be used for this patient:

- American Society of Anesthesiologists standard monitors, including multiple-lead ST-segment analysis
- Temperature
- Direct arterial blood pressure
- Transesophageal echocardiography or esophageal cardiac output probe if general anesthesia is planned.

C.2. What anesthetic technique is preferable for patients undergoing TURP, and why?

Regional anesthesia is assumed to be the best anesthetic technique for patients undergoing monopolar electrode TURP for the following reasons:

- It allows monitoring of the patient's mentation, thereby facilitating early detection of signs of TURP syndrome.
- It promotes vasodilation and peripheral pooling of blood, thereby reducing the severity of circulatory overloading.
- It reduces blood loss by lowering blood pressure during surgery.
- It provides postoperative analgesia, thereby reducing the incidence of postoperative hypertension and tachycardia, which often accompanies recovery from general anesthesia.

- Currently, less emphasis is placed on regional anesthesia (vs. general anesthesia) for TURP because of the increased use of bipolar electrode and laser resection surgical techniques.
- Regional anesthesia may not be a safe option in an anticoagulated patient.

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1365–1368.

Malhotra V. Transurethral resection of prostate. *Anesthesiol Clin North America*. 2000;18: 883–897.

Miller RD, Eriksson LI, Fleisher LA, et al., eds. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:2119–2123.

C.3. Does regional anesthesia result in a lower incidence of perioperative mortality than general anesthesia? Whether yes or no, explain why or why not.

Although spinal anesthesia offers distinct advantages over general anesthesia for TURP surgery, mortality and many markers of patient outcome have been similar for both groups. The 30-day mortality rate associated with TURP was reported to be between 0.4% and 2.5% in 2000 and was dependent on the age of the patient. Mortality rates are reported to be similar in patients receiving regional anesthesia or general anesthesia. Increased morbidity was found in patients with resections exceeding 90 minutes, gland size greater than 45 g, acute urinary retention, and age older than 80 years. The incidence of postoperative complications, specifically MI, pulmonary embolism, cerebrovascular accidents, transient ischemic attacks, renal failure, hepatic insufficiency, and the need for prolonged ventilation, is similar in patients receiving regional anesthesia and those receiving general anesthesia. More recently, with the use of bipolar electrode and laser TURP resection surgical techniques, it is believed that mortality rates will likely decline.

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1365–1368.

Hawary A, Mukhtar K, Sinclair A, et al. Transurethral resection of the prostate syndrome: almost gone but not forgotten. *J Endourol*. 2009;23:2013–2020.

Malhotra V. Transurethral resection of prostate. *Anesthesiol Clin North Am*. 2000;18: 883–897.

Miller RD, Eriksson LI, Fleisher LA, et al., eds. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:2119–2123.

Wasson JH, Bubolz TA, Lu-Yao GL, et al. Transurethral resection of the prostate among medicare beneficiaries: 1984 to 1997. For the Patient Outcomes Research Team for Prostatic Diseases. *J Urol*. 2000;164:1212–1215.

C.4. What intravenous fluid would you use during TURP?

Because dilutional hyponatremia commonly occurs in patients undergoing monopolar electrode TURP, the intravenous fluid of choice perioperatively is normal saline that contains sodium, 154 mEq per L. It is important to remember, however, that circulatory overloading from absorbed irrigant is common in patients who have undergone monopolar or bipolar electrode TURP (but not laser TURP); therefore, the amount of intravenous fluid administered during surgery should be carefully monitored.

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1365–1368.

Hai MA, Malek RS. Photoselective vaporization of the prostate: initial experience with a new 80 W KTP Laser for the treatment of benign prostatic hyperplasia. *J Endourol*. 2003;17:93–96.

Malek RS, Kuntzman RS, Barrett DM. High-power potassium-titanyl-phosphate laser vaporization prostatectomy. *J Urol*. 2000;163:1730–1733.

C.5. Forty minutes after a sensory level of T-10 was established with intrathecal anesthesia, and monopolar TURP resection was initiated with the use of glycine as the bladder irrigating solution, the patient becomes agitated and complains of nausea. Further sedation along with an antiemetic are administered. However, shortly thereafter, the patient becomes very restless, blood pressure rises, and heart rate decreases. The patient becomes cyanotic and obtunded, blood pressure precipitously falls, pupils are dilated and unresponsive to light. What is the most likely cause of these signs and symptoms, and would these occur during bipolar or laser TURP resection?

Restlessness and incoherence during TURP are particularly ominous signs of TURP syndrome. These are often caused by subtle pulmonary edema, hypoxemia, and cerebral edema. These signs must not be misinterpreted as signs of inadequate anesthesia. The administration of sedatives or general anesthesia in the presence of TURP syndrome is often fraught with severe complications, even death. In bipolar and laser TURP, normal saline can be used as the bladder irrigating solution and hyponatremia is not expected. In bipolar TURP, absorption of the intravascular bladder irrigating solution can occur via the prostatic venous sinusis, but is not expected in laser TURP.

Bogdan G, Razvan M, Mihai D, et al. Transurethral resection (TUR) in saline plasma vaporization of the prostate vs standard TUR of the prostate: the better choice in benign prostatic hyperplasia? *BJU International*. 2010;106(11):1695–1699.

Gravenstein D. Transurethral resection of the prostate (TURP) syndrome: a review of the pathophysiology and management. *Anesth Analg*. 1997;84:438–446.

Qi Chen, Li Zhang, Qi-Liang Fan, et al. Bipolar transurethral resection in saline vs traditional monopolar resection of the prostate: results of a randomized trial with a 2-year follow-up. *BJU International*. 2010;106(9):1339–1343.

C.6. What are the important characteristics of irrigation solutions used during TURP?

Ideal TURP irrigation solutions are either isotonic or nearly isotonic, electrically inert, nontoxic, and transparent. Electrolyte-containing solutions are avoided in monopolar electrode TURP because they can conduct electrical current to surrounding tissues and cause burns. Because significant absorption of bladder irrigating solution can occur during TURP, only solutions with nontoxic solutes are used. The solution must be transparent to allow the surgeon to visualize the surgical site. If intravascular hypotonic bladder irrigating solution is absorbed, absorption can lead to hyponatremia, hypoosmolality, and, in severe cases, hemolysis. These complications are avoided when normal saline is used with bipolar electrode and laser resection TURP.

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1365–1368.

Gravenstein D. Transurethral resection of the prostate (TURP) syndrome: a review of the pathophysiology and management. *Anesth Analg*. 1997;84:438–446.

Malhotra V. Transurethral resection of prostate. *Anesthesiol Clin North America*. 2000;18: 883–897.

C.7. Why is plain distilled water rarely used for irrigation during TURP? What types of irrigation solutions are available?

Although distilled water is totally transparent and electrically inert and was regularly used decades ago for irrigation during monopolar TURP, it is extremely hypotonic. Therefore, when it is absorbed, it may cause hemolysis, shock, and renal failure.

Over the years, a number of isotonic and nearly isotonic irrigation solutions have been introduced and they have almost totally replaced plain distilled water. The most commonly used solution is currently glycine (1.2% and 1.5%). Mannitol (3%), glucose (2.5% to 4%), Cytal (a mixture of sorbitol 2.7% and mannitol 0.54%), and urea (1%) solutions are also occasionally used. For maintenance of their transparency, these solutions are purposely prepared moderately hypotonic. Sterile water and glycine have been used as the bladder irrigation solution in laser resection TURP because they are minimally absorbed, but TURP syndrome has been reported when bladder perforation or urethral trauma occurred.

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1365–1368.

Dilger JA, Walsh MT, Warner ME, et al. Urethral injury during potassium-titanyl-phosphate laser prostatectomy complicated by transurethral resection syndrome. *Anesth Analg*. 2008;107:1438–1440.

Farag E, Baccala AA Jr., Doutt RF, et al. Laser bladder perforation from photoselective vaporization of prostate resulting in rhabdomyolysis induced acute renal failure. *Minerva Anesthesiol*. 2008;74:277–280.

Gravenstein D. Transurethral resection of the prostate (TURP) syndrome: a review of the pathophysiology and management. *Anesth Analg*. 1997;84:438–446.

Malhotra V. Transurethral resection of prostate. *Anesthesiol Clin North America*. 2000;18: 883–897.

Miller RD, Eriksson LI, Fleisher MD, et al. *Miller's Anesthesia* 7th ed. Philadelphia: Churchill Livingstone; 2010:2119–2123.

C.8. What is the effect on body temperature of continuous bladder irrigation during TURP?

Several liters of irrigation solution pass through the bladder during TURP. This can reduce body temperature at the rate of 1° C per hour (Fig. 24.1). Approximately half the patients undergoing TURP become hypothermic and shiver at the conclusion of surgery.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1365–1368.

Malhotra V. Transurethral resection of prostate. *Anesthesiol Clin North America*. 2000;18: 883–897.

Miller RD, Eriksson LI, Fleisher MD, et al. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:2119–2123.

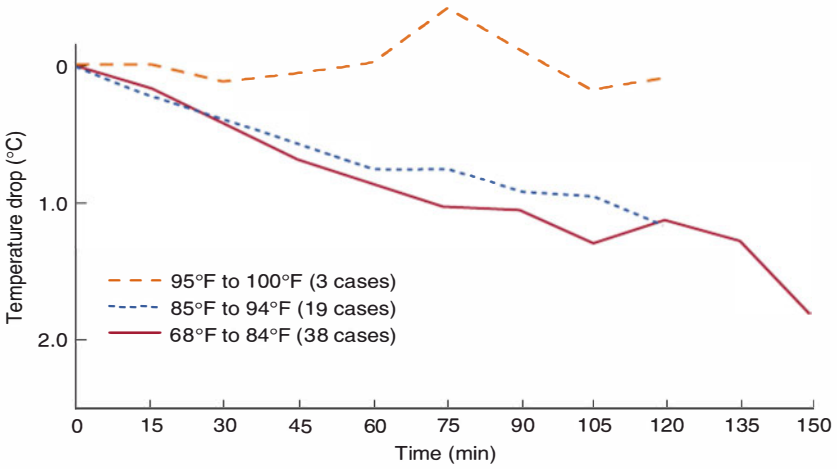

Figure 24.1 The decrease in body temperature during transurethral resection of the prostate (TURP) is related to the temperature of the irrigating solution and to the duration of surgery. (From Allen TD. Body temperature changes during prostatic resection as related to the temperature of the irrigating solution. *J Urol.* 1973;110:433–535, with permission.)

C.9. What is the definition of TURP syndrome? What are the signs and symptoms of the syndrome?

Rapid absorption of a large-volume, mainly hypotonic bladder irrigation solution during TURP can lead to TURP syndrome. TURP syndrome is characterized by intravascular volume shifts and plasma-solute (osmolarity) effects. The signs and symptoms of TURP syndrome are as follows:

Cardiopulmonary

Hypertension
Bradycardia
Dysrhythmia
Respiratory distress
Cyanosis
Hypotension
Shock
Death

Hematologic and renal

Hyperglycinemia
Hyperammonemia
Hyponatremia
Hypoosmolality
Hemolysis/anemia
Acute renal failure
Death

Central nervous system

Nausea/vomiting
Confusion/restlessness

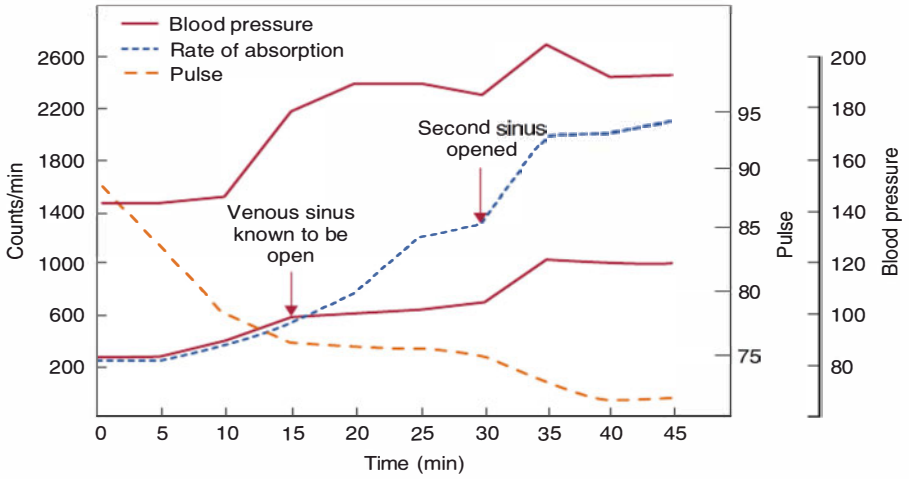

Figure 24.2 The blood pressure, heart rate, and absorption rate of radioactively tagged irrigation solution during transurethral resection of the prostate. (From Taylor RO, Maxson ES, Carter FH, et al. Volumetric gravimetric and radioisotopic determination of fluid transference in transurethral prostatectomy. *J Urol.* 1958;79:490–499, with permission.)

Blindness
Twitches/seizures
Lethargy/paralysis
Dilated/nonreactive pupils
Coma
Death

TURP syndrome can occur as early as a few minutes after surgery has started and as late as several hours after surgery. Patient complaints of dizziness, headache, nausea, chest or throat tightness, and shortness of breath are often early clinical signs. Then the patient becomes restless, confused, and starts to retch. Some patients complain of abdominal pain. The blood pressure often rises (both systolic and diastolic), and the heart rate decreases (Fig. 24.2). If not treated promptly, the patient becomes cyanotic and hypotensive and ultimately sustains cardiac arrest.

Occasionally, TURP syndrome manifests as neurologic signs. The patient becomes lethargic, then unconscious; and pupils dilate, reacting sluggishly to light. These signs may be followed by short episodes of tonic–clonic seizures and then coma lasting from minutes to hours.

If the patient is under general anesthesia, the presenting signs of TURP syndrome are typically a rise and then a fall in blood pressure, decreasing oxygen saturation, and severe refractory bradycardia. The ECG may show nodal rhythm, ST-segment changes, U waves, and widening of the QRS complex. Recovery from general anesthesia is usually delayed.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia.* 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1365–1368.

Gravenstein D. Transurethral resection of the prostate (TURP) syndrome: a review of the pathophysiology and management. *Anesth Analg.* 1997;84:438–446.

Henderson DJ, Middleton RG. Coma from hyponatremia following transurethral resection of prostate. *Urology.* 1980;15:267–271.

Hurlbert BJ, Wingard DW. Water intoxication after 15 minutes of transurethral resection of the prostate. *Anesthesiology*. 1979;50:355–356.

Malhotra V. Transurethral resection of prostate. *Anesthesiol Clin North America*. 2000;18:883–897.

Miller RD, Eriksson LI, Fleisher MD, et al. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:2119–2123.

Roesch RP, Stoelting RK, Lingeman JE, et al. Ammonia toxicity resulting from glycine absorption during a transurethral resection of the prostate. *Anesthesiology*. 1983:58:577–579.

Still AJ, Modell JA. Acute water intoxication during transurethral resection of the prostate using glycine solution for irrigation. *Anesthesiology*. 1973;38:98–99.

C.10. How can hyponatremia occur if the bladder irrigating fluid is not absorbed via the prostatic vessels?

If the complication of bladder perforation occurs, significant accumulation of irrigating fluid in the intraperitoneal or extraperitoneal (retroperitoneal) space can occur, resulting in significant intravascular absorption of a hypotonic irrigating solution and ultimately hyponatremia syndrome.

Dorotta I, Basali A, Ritchey M, et al. Transurethral resection syndrome after bladder perforation. *Anesth Analg*. 2003;97:1536–1568.

C.11. How does the patient absorb irrigation solution during TURP? How much irrigation solution is typically absorbed?

The bladder irrigation solution enters the bloodstream directly through open prostatic venous sinuses created during monopolar and bipolar resection techniques, and it accumulates in the periprostatic and retroperitoneal spaces. The latter accumulation occurs primarily when the prostatic capsule is violated during surgery.

Reports in the literature suggest that as many as 8 L of irrigation solution can be absorbed by the patient during TURP. The average rate of absorption is 20 mL per minute and may reach 200 mL per minute; the average weight gain by the end of surgery is 2 kg (Fig. 24.3). A very thin resection "zone" combined with a coagulating benefit during laser TURP prevents significant opening of the prostatic venous sinuses and absorption of the irrigating solution.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1365–1368.

Masloff JI, Milam JH, Bunts RC. Fluid and electrolyte changes associated with transurethral prostatic resection. *South Med J*. 1966;59:1203–1208.

Oester A, Madsen PO. Determination of absorption of irrigating fluid during transurethral resection of the prostate by means of radioisotope. *J Urol*. 1969;102:714–719.

C.12. How can one estimate the volume of irrigation solution absorbed during TURP?

A practical method for estimating the absorbed volume of irrigation solution during TURP is based on the following equation:

$$\text{Volume absorbed} = \frac{\text{preoperative } [Na^+]}{\text{postoperative } [Na^+]} \times \text{extracellular fluid} - \text{extracellular fuild}$$

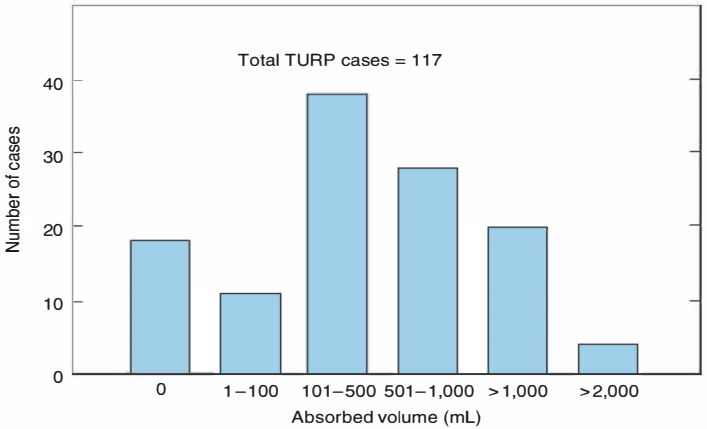

Figure 24.3 The volume of irrigation solution absorbed during transurethral resection of the prostate. (From Madsen PO, Madsen RE. Clinical and experimental evaluation of different irrigating fluids for transurethral surgery. *Invest Urol.* 1965;3:122–129, with permission.)

To use this equation, serum sodium level ($[Na^+]$) is determined at the beginning of surgery and again at the time when the volume absorbed is estimated. The extracellular fluid (ECF) volume is assumed to be 20% to 30% of body weight. For example, if the patient's preoperative body weight is 60 kg and the ECF is assumed to constitute 20% of the patient's body weight, then a decrease in serum sodium level from 140 to 100 mEq per L would suggest an absorption of 4.8 L:

$$140/100 \times ECF - ECF = 1.4\ ECF - ECF = 0.4\ ECF = 0.4 \times 60 \times 20\% = 4.8L$$

Henderson DJ, Middleton RG. Coma from hyponatremia following transurethral resection of prostate. *Urology.* 1980;15:267–271.

Piros D, Fagerstrom T, Collins JW, et al. Glucose as a marker of fluid absorption in bipolar transurethral surgery. *Anesth Analg.* 2009;109:1850–1855.

C.13. What is the relation between the duration of surgery and the incidence of TURP syndrome?

Many believe that the duration of surgery is the most important determinant in the incidence of TURP syndrome. However, several studies report severe TURP syndrome occurring as early as 15 to 20 minutes after surgery has started. In general, a poor correlation has been observed between the duration of surgery and the amount of irrigation solution absorbed. In a large series, morbidity and mortality of patients undergoing TURP did not correlate with length of surgery, except when surgery lasted more than 150 minutes. Similarly, the incidence and severity of hyponatremia did not correlate with the duration of surgery.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia.* 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1365–1368.

Malhotra V. Transurethral resection of prostate. *Anesthesiol Clin North America.* 2000;18: 883–897.

Miller RD, Eriksson LI, Fleisher MD, et al. *Miller's Anesthesia.* 7th ed. Philadelphia: Churchill Livingstone; 2010:2119–2123.

C.14. What factors increase the incidence of TURP syndrome?

TURP syndrome is more likely to occur if the prostatic gland is atypically large, the prostatic capsule is violated during surgery, or the hydrostatic pressure of the irrigation solution is excessively high. Large prostatic glands have rich venous networks that promote intravascular absorption of irrigation solution. The violation of the prostatic capsule during surgery promotes entry of irrigation solution into the periprostatic and retroperitoneal spaces. The hydrostatic pressure of the irrigation solution is an important determinant of the rate at which the patient will absorb the solution. This pressure depends primarily on the height of the irrigation solution pole. When the height of the pole exceeds 60 cm (~2 ft), the absorption of irrigation solution is greatly enhanced. Also, an excessively distended bladder during surgery facilitates absorption.

Gravenstein D. Transurethral resection of the prostate (TURP) syndrome: a review of the pathophysiology and management. *Anesth Analg.* 1997;84:438–446.

Logie JRC, Keenan RA, Whiting PH, et al. Fluid absorption during transurethral prostatectomy. *J Urol.* 1980;52:526–528.

Malhotra V. Transurethral resection of prostate. *Anesthesiol Clin North America.* 2000;18:883–897.

Miller RD, Eriksson LI, Fleisher MD, et al. *Miller's Anesthesia.* 7th ed. Philadelphia: Churchill Livingstone; 2010:2119–2123.

C.15. What is the effect on cardiopulmonary, renal, and central nervous system (CNS) functions of excessive absorption of irrigation solution during TURP?

Excessive absorption of irrigation solution during TURP causes hypervolemia and hypertension and may induce angina and pulmonary edema (Fig. 24.4). It may also have an adverse effect on renal function. An inverse relation has been observed between the amount of irrigation solution absorbed during surgery and postoperative urinary output.

Some patients with TURP syndrome exhibit neurologic signs resulting from water intoxication. They assume a decerebrate posture, exhibit clonus and positive Babinski reflex, and eventually convulse and lapse into coma. Examination of the eyes reveals papilledema and dilated and sluggishly reacting pupils. The electroencephalogram shows low voltage bilaterally. The patients may remain in a coma from a few hours to several days.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia.* 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1365–1368.

Casthely P, Ramanathan S, Chalon J, et al. Decrease in electric impedance during transurethral resection of the prostate: an index of early water intoxication. *J Urol.* 1981;125:347–349.

Gravenstein D. Transurethral resection of the prostate (TURP) syndrome: a review of the pathophysiology and management. *Anesth Analg.* 1997;84:438–446.

Malhotra V. Transurethral resection of prostate. *Anesthesiol Clin North America.* 2000;18:883–897.

Miller RD, Eriksson LI, Fleisher MD, et al. *Miller's Anesthesia.* 7th ed. Philadelphia: Churchill Livingstone; 2010:2119–2123.

C.16. What causes CNS dysfunction in patients who have undergone TURP?

The crucial physiologic derangement of CNS function is not hyponatremia per se, but acute hypoosmolality, which is predictable because the blood–brain barrier is essentially

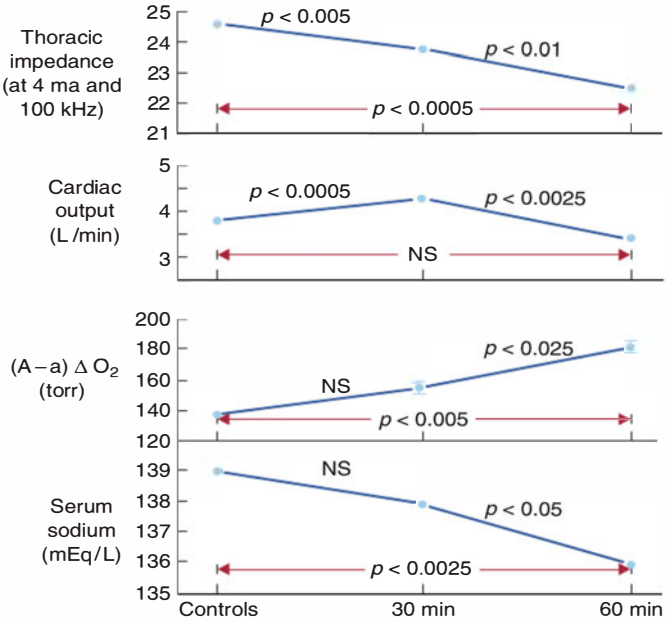

Figure 24.4 Mean changes in thoracic impedance, cardiac output, alveolar–arterial oxygen tension difference, and serum sodium level during transurethral resection of the prostate; NS = nonsignificant. (From Casthely P, Ramanathan S, Chalon J, et al. Decrease in electric impedance during transurethral resection of the prostate: an index of early water intoxication. *J Urol.* 1981;125:347–349, with permission.)

impermeable to sodium but freely permeable to water. Cerebral edema caused by acute hypoosmolality can increase intracranial pressure, which results in bradycardia and hypertension by the Cushing reflex. Furthermore, cerebral edema is not caused by decreased serum colloid oncotic pressure, but by decreased osmolality. Apparently, the hypervolemia and hyponatremia that often accompany TURP promote cerebral edema and this in turn raises intracranial pressure and induces neurologic symptoms. The rise in intracranial pressure is directly related to the gain in body weight during TURP.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia.* 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1365–1368.

Gravenstein D. Transurethral resection of the prostate (TURP) syndrome: a review of the pathophysiology and management. *Anesth Analg.* 1997;84:438–446.

Malhotra V. Transurethral resection of prostate. *Anesthesiol Clin North America.* 2000;18: 883–897.

C.17. What is the physiologic role of sodium ions in the body? What is the effect of excessive absorption of irrigation solution on serum sodium level?

Sodium is a ubiquitous electrolyte that is essential for proper function of excitatory cells, particularly those of the heart and brain. Extreme reduction in serum sodium level alters brain, cardiac, and renal functions.

During monopolar TURP, serum sodium level typically falls 3 to 10 mEq per L. However, the correlation between the severity of hyponatremia and the amount of irrigation solution absorbed during surgery is inconsistent. The fall in serum sodium level apparently depends primarily on the rate at which the irrigation solution is absorbed rather than on the total amount absorbed.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia.* 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1365–1368.

Hahn RG. Relations between irrigation absorption rate and hyponatraemia during transurethral resection of the prostate. *Acta Anaesthesiol Scand.* 1988;32:53–60.

Malhotra V. Transurethral resection of prostate. *Anesthesiol Clin North America.* 2000;18:883–897.

Rhymer JC, Bell TJ, Perry KC, et al. Hyponatremia following transurethral resection of the prostate. *Br J Urol.* 1985;57:450–452.

C.18. What is the relation between serum sodium level and the incidence of neurologic symptoms in patients who have undergone TURP?

Acute severe hyponatremia is often associated with abnormal neurologic symptoms, and it can lead to irreversible brain damage. The neurologic signs may be accompanied by electroencephalogram abnormalities such as loss of α-wave activity and irregular discharge of high-amplitude slow-wave activity. However, the correlation between the severity of the hyponatremia and the incidence of neurologic symptoms is inconsistent because hyponatremia may not be the sole or even primary cause of the neurologic manifestations of TURP syndrome. The crucial derangement of CNS function is not hyponatremia per se, but acute hypoosmolarity. In some cases, moderate hyponatremia is associated with severe neurologic symptoms; in others, severe hyponatremia manifests no symptoms at all. Apparently, the factor governing the manifestation of symptoms is the rate at which the serum sodium level falls rather than the total fall itself. The faster the fall in serum sodium level, the greater the incidence of neurologic symptoms. A slow fall in serum sodium level apparently allows the CNS to adapt to the hyponatremia.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia.* 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1365–1368.

Gravenstein D. Transurethral resection of the prostate (TURP) syndrome: a review of the pathophysiology and management. *Anesth Analg.* 1997;84:438–446.

Henderson DJ, Middleton RG. Coma from hyponatremia following transurethral resection of prostate. *Urology.* 1980;15:267–271.

Malhotra V. Transurethral resection of prostate. *Anesthesiol Clin North America.* 2000;18:883–897.

C.19. How does acute hyponatremia affect the cardiovascular system?

When serum sodium level falls to less than 120 mEq per L, signs of cardiovascular depression can occur. A decrease of less than 115 mEq per L causes bradycardia, widening of the QRS complex, ST-segment elevation, ventricular ectopic beats, and T-wave inversion. Patients with a serum sodium level of less than 110 mEq per L can develop respiratory and cardiac arrest.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia.* 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1365–1368.

Logie JRC, Keenan RA, Whiting PH, et al. Fluid absorption during transurethral prostatectomy. *J Urol.* 1980;52:526–528.

Malhotra V. Transurethral resection of prostate. *Anesthesiol Clin North America*. 2000;18: 883–897.

Mebust WK, Brady TW, Valk WL. Observations on cardiac output, blood volume, central venous pressure, fluid and electrolyte changes in patients undergoing transurethral prostatectomy. *J Urol*. 1970;103:632–636.

Osborn DE, Rao PN, Green MJ, et al. Fluid absorption during transurethral resection. *Br Med J*. 1980;281:1549–1550.

Surawicz B. Relationship between electrocardiogram and electrolytes. *Am Heart J*. 1967;73:814–834.

C.20. What prophylactic measures may reduce the incidence of TURP syndrome?

The incidence of TURP syndrome depends primarily on the surgeon's technical skills. However, if the patient is properly prepared before surgery and closely monitored during surgery, the incidence and severity of the syndrome can be reduced.

Fluid and electrolyte imbalance should be corrected preoperatively and special attention should be paid to the serum sodium especially in traditional monopolar electrode TURP. Patients with preoperative CHF should be treated vigorously with diuretics and fluid restriction. A conservative surgical approach should be considered for critically ill patients. A simple canalization or balloon dilation of the urethra or a staged TURP is less likely to induce TURP syndrome.

The most important preventive measure during surgery is preservation of the prostatic capsule. Another preventive measure is restriction of the hydrostatic pressure of the irrigation solution to 60 cm H_2O. This can be accomplished by maintaining the height of the irrigation pole to 60 cm (~2 ft) above patient level. Also, the bladder should not be allowed to overdistend and the duration of surgery should be restricted.

Serial serum sodium and osmolality are advisable in order to detect a decreasing trend. If clinical signs of TURP syndrome present, the surgeon should be informed and therapeutic measures immediately instituted. If serum sodium level approaches 120 mEq per L, surgery should be terminated as soon as possible.

Intravenous fluids should be cautiously administered during TURP. A microdrip is recommended particularly for patients with cardiac or renal disease. If regional anesthesia causes hypotension, a small dose of a vasoconstrictor is recommended to raise the blood pressure, rather than rapid infusion of intravenous fluids.

Gravenstein D. Transurethral resection of the prostate (TURP) syndrome: a review of the pathophysiology and management. *Anesth Analg*. 1997;84:438–446.

Malhotra V. *Anesthesia for Renal and Genituourologic Surgery*. New York: McGraw-Hill; 1996:93–109.

Watkins-Pitchford JM, Payne SR, Rennie CD, et al. Hyponatremia during transurethral resection. Its practical prevention. *Br J Urol*. 1984;56:676–678.

C.21. What therapeutic measures are recommended for patients with TURP syndrome?

When symptoms of TURP syndrome appear, the following therapeutic measures are recommended:

- Terminate surgery as soon as possible.
- Administer furosemide, 20 mg intravenously.
- Administer oxygen by nasal cannula or face mask to maintain oxygen saturation and consider intubation.
- Obtain arterial blood gas, serum osmolality, and sodium analysis.

- If the serum sodium level is abnormally low and clinical signs of hyponatremia are evident, intravenous administration of hypertonic saline (3% to 5%) may be recommended. The hypertonic solution should be given at a rate no faster than 100 mL per hour. In most cases, no more than 300 mL of saline is needed to correct the hyponatremia.
- If the patient develops seizures, a short-acting anticonvulsant such as diazepam (5 to 20 mg) or midazolam (2 to 10 mg) can be administered intravenously. If these drugs do not arrest the seizures, a barbiturate or phenytoin can be added. As a last resort, a muscle relaxant may also be used.
- If pulmonary edema or hypotension develops, invasive hemodynamic monitoring is recommended. This will serve as a guide for pharmacologic support and fluid administration.
- If significant blood loss is suspected, the administration of packed red blood cells should be considered. In general, intravenous fluids should be administered cautiously because of the propensity of these patients to develop pulmonary edema.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia.* 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1365–1368.

Malhotra V. Transurethral resection of prostate. *Anesthesiol Clin North America.* 2000;18: 883–897.

Miller RD, Eriksson LI, Fleisher MD, et al. *Miller's Anesthesia.* 7th ed. Philadelphia: Churchill Livingstone; 2010:2119–2123.

C.22. Is normal saline administration always necessary to correct hyponatremia? Explain. What are the risks of rapidly correcting hyponatremia?

The administration of hypertonic saline to correct hyponatremia is not always necessary and sometimes can be detrimental. Unless the patient develops clinical signs of hyponatremia, saline administration is not recommended. Spontaneous or induced diuresis usually corrects the hyponatremia within a few hours.

Patients who have undergone TURP often sustain circulatory overloading during surgery; consequently, saline administration in these patients can induce pulmonary edema. In addition, rapid administration of hypertonic saline has been associated with central pontine myelinolysis (osmotic demyelination syndrome)—a poorly understood and fatal neurologic complication.

To reduce the hazards of saline administration, serum osmolarity should be monitored and corrected aggressively only until symptoms substantially subside; then hyponatremia should be corrected at a rate no faster than 1.5 mEq/L/hour.

Gravenstein D. Transurethral resection of prostate (TURP) syndrome: a review of pathophysiology and management. *Anesth Analg.* 1997;84:438–446.

Rothenberg DM, Berns AS, Ivankovich AD. Isotonic hyponatremia following transurethral prostate resection. *J Clin Anesth.* 1990;2:48–53.

Sterns RH, Riggs JE, Schochet SS Jr. Osmotic demyelinization syndrome following correction of hyponatremia. *N Engl J Med.* 1986;314:1535–1542.

C.23. What are the toxic effects of glycine? Is there an antidote to glycine toxicity? What are the metabolic byproducts of glycine?

Glycine is an inhibitory neurotransmitter similar to γ-aminobutyric acid in the spinal cord and brain. When absorbed by the patient in large amounts, glycine has direct toxic effects on the heart and retina. In patients who have undergone TURP with

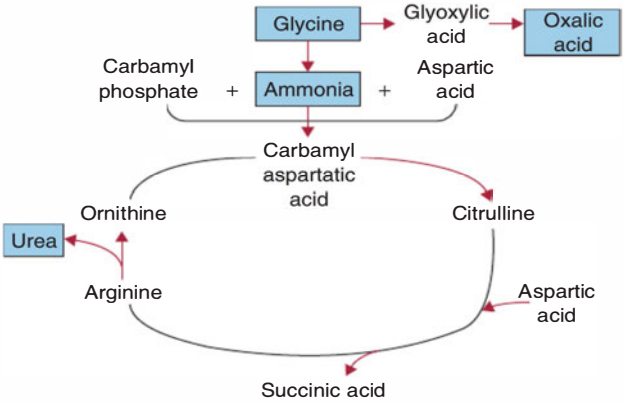

Figure 24.5 Metabolic pathways of glycine. (From McGilvery RW, Goldstein GW. *Biochemistry: A Functional Approach.* 3rd ed. Philadelphia: WB Saunders; 1983:584, with permission.)

glycine absorption, it has been shown to cause an average decrease of 17.5% in cardiac output. In animal studies, the administration of the amino acid arginine reversed the myocardial depressing effect of glycine. The mechanism by which glycine depresses cardiac function and the mechanism by which arginine protects the heart is unknown.

Hyperglycinemia may cause transient visual disturbance (blindness) during TURP. However, glycine toxicity in patients who have undergone TURP is uncommon, probably because most of the absorbed glycine is retained in the periprostatic and retroperitoneal spaces, where access to the circulation is limited.

The most common metabolites of glycine are ammonia and glyoxylic and oxalic acids (Fig. 24.5). In some patients, excessive absorption of glycine during TURP leads to hyperammonemia. Hyperoxaluria could compromise renal function in patients with coexisting renal disease, which is often present in elderly patients undergoing TURP.

Glycine may cause encephalopathy and seizures through its ability to potentiate the effects of *N*-methyl-D-aspartate, an excitatory neurotransmitter. Magnesium exerts a negative control on the *N*-methyl-D-aspartate receptor, and hypomagnesemia caused by dilution may increase the susceptibility to seizures. For this reason, a trial of magnesium therapy may be indicated in patients who develop seizures during TURP.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia.* 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1365–1368.

Gravenstein D. Transurethral resection of the prostate (TURP) syndrome: a review of the pathophysiology and management. *Anesth Analg.* 1997;84:438–446.

Malhotra V. Transurethral resection of prostate. *Anesthesiol Clin North America.* 2000;18: 883–897.

McGilvery RW, Goldstein GW. *Biochemistry: A Functional Approach.* 3rd ed. Philadelphia: WB Saunders; 1983:584.

Miller RD, Eriksson LI, Fleisher MD, et al. *Miller's Anesthesia.* 7th ed. Philadelphia: Churchill Livingstone; 2010:2119–2123.

Ovassapian A, Joshi CW, Brumer EA. Visual disturbances: an unusual symptom of transurethral prostatic resection reaction. *Anesthesiology.* 1982;57:332–334.

Wang JM, Wong KC, Creel DJ, et al. Effects of glycine on hemodynamic responses and visual evoked potentials in the dog. *Anesth Analg.* 1985;64:1071–1077.

C.24. What are the symptoms and clinical course of TURP-induced hyperammonemia?

The signs and symptoms of hyperammonemia usually appear within 1 hour of surgery. Typically, the patient becomes nauseated, vomits, and then becomes comatose. Blood ammonia level rises to more than 500 mmol per L. The patient remains comatose for 10 to 12 hours and eventually awakens when ammonia blood level decreases to less than 150 mmol per L. The hyperammonemia tends to linger postoperatively, probably because glycine absorption from the periprostatic space continues after surgery.

Malhotra V. Transurethral resection of prostate. *Anesthesiol Clin North America.* 2000;18: 883–897.

Oester A, Madsen PO. Determination of absorption of irrigating fluid during transurethral resection of the prostate by means of radioisotope. *J Urol.* 1969;102:714–719.

C.25. Why do some patients who have undergone TURP develop hyperammonemia and others do not? Is there a preventive treatment for hyperammonemia in these patients?

Because ammonia is metabolized primarily in the liver, it has been speculated that hyperammonemia after TURP is a result of liver dysfunction. However, liver dysfunction has not been found in these patients. Further, there is no evidence that patients with a known liver dysfunction are susceptible to hyperammonemia after TURP.

A more plausible explanation for the hyperammonemia is arginine deficiency. Normally, the ornithine cycle in the liver converts ammonia to urea (see Fig. 24.5). Arginine is an important intermediate product of this cycle. Apparently, patients who have undergone TURP while having arginine deficiency cannot detoxify the excess ammonia produced from glycine metabolism, and they therefore develop hyperammonemia. The time necessary to deplete the endogenous arginine stores may be as brief as 12 hours, which approximates the preoperative fasting time.

Several studies support this hypothesis. In dogs, the administration of arginine concurrently with glycine reduced the secretion of ammonia by the liver (Fig. 24.6). In humans, prophylactic administration of arginine or ornithine prevents hyperammonemia that otherwise follows rapid intravenous administration of glycine. Routine administration of arginine in patients undergoing TURP, however, is not recommended because they rarely develop hyperammonemia.

Fahey JL. Toxicity and blood ammonia rise resulting from intravenous amino acid administration in man: the protective effect of l-arginine. *J Clin Invest.* 1957;36:1647–1655.

Fahey JL, Perry RS, McCoy PF. Blood ammonia elevation and toxicity from intravenous L-amino acid administration to dogs: the protection role of L-arginine. *Am J Physiol.* 1958;192:311–317.

Gravenstein D. Transurethral resection of the prostate (TURP) syndrome: a review of the pathophysiology and management. *Anesth Analg.* 1997;84:438–446.

Nathans D, Fahey JL, Ship AG. Sites of origin and removal of blood ammonia formed during glycine infusion: effect of L-arginine. *J Lab Clin Med.* 1958;51:124–133.

Roesch RP, Stoelting RK, Lingeman JE, et al. Ammonia toxicity resulting from glycine absorption during a transurethral resection of the prostate. *Anesthesiology.* 1983; 58:577–579.

Ryder KW, Olson JF, Khanoski RJ, et al. Hyperammonemia after transurethral resection of the prostate: a report of 2 cases. *J Urol.* 1984;132:995–997.

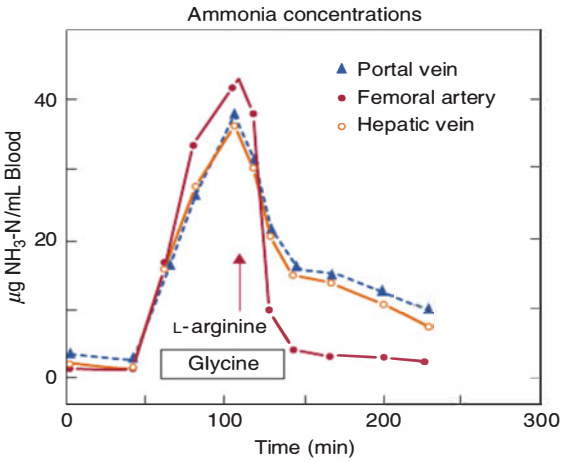

Figure 24.6 Ammonia blood levels during glycine administration in dogs before and after arginine supplementation. (From Nathans D, Fahey JL, Ship AG. Sites of origin and removal of blood ammonia formed during glycine infusion: effect of L-arginine. *J Lab Clin Med.* 1958;51:124–133, with permission.)

C.26. What are the clinical characteristics, causes, and prognosis of TURP-related blindness?

Transient blindness is one of the more alarming complications of TURP. The patient complains of blurred vision and of seeing halos around objects. This can occur either during surgery or later in the recovery room. Although it is sometimes accompanied by other TURP-related complications, the blindness usually occurs as an isolated symptom. Examination of the eyes reveals dilated and unresponsive pupils. Postoperatively, TURP-related blindness gradually recedes and eyesight returns to normal within 8 to 48 hours of surgery.

The cause of TURP-related blindness is unclear. The intraocular pressure and optic discs remain normal. In the past, edema of the cerebral optical cortex was suspected; however, the clinical signs of TURP-related blindness are consistent with retinal rather than cortical dysfunction. Unlike cortical blindness, TURP-related blindness allows perception of light and the blink reflex is preserved. TURP-related blindness is most likely caused by a toxic effect of glycine on the retina. This theory is supported by the fact that glycine is a known inhibitory neurotransmitter. In animals, glycine has been shown to inhibit neuronal visual pathways. Also, the severity of TURP-related blindness is directly related to glycine blood level. Postoperatively, vision gradually improves as the glycine blood level declines.

Defalque RJ, Miller DW. Visual disturbances during transurethral resection of the prostate. *Can Anaesth Soc J*. 1975;22:620–621.

Gravenstein D. Transurethral resection of the prostate (TURP) syndrome: a review of the pathophysiology and management. *Anesth Analg.* 1997;84:438–446.

Malhotra V. Transurethral resection of prostate. *Anesthesiol Clin North America.* 2000;18: 883–897.

Ovassapian A, Joshi CW, Brumer EA. Visual disturbances: an unusual symptom of transurethral prostatic resection reaction. *Anesthesiology.* 1982;57:332–334.

C.27. What gynecologic procedure has been associated with a syndrome similar to TURP syndrome?

Hysteroscopy has been associated with symptoms not unlike those of TURP syndrome. The procedure involves visualization of the interior lining of the uterus for diagnostic purposes and, on occasion, for transcervical resection of the endometrium or submucous myomectomy. The latter often requires electrical cauterization. As with TURP, hysteroscopy requires irrigation with nonionic isotonic solutions. Commonly used solutions contain either glucose or glycine. Side effects such as hyponatremia, hyperglycemia, circulatory overloading, and coagulopathy have been reported.

Carson SA, Hubert GD, Schriock ED, et al. Hyperglycemia and hyponatremia during operative hysteroscopy with 5% dextrose in water distention. *Fertil Steril.* 1989; 51:341–343.

Goldenberg M, Zolti M, Seidman DS, et al. Transient blood oxygen desaturation, hypercapnia, and coagulopathy after operative hysteroscopy with glycine used as the distending medium. *Am J Obstet Gynecol.* 1994;170:25–29.

C.28. What are the causes of excessive bleeding during TURP?

Patients undergoing TURP commonly bleed perioperatively. One possible cause is dilutional thrombocytopenia resulting from excessive absorption of irrigation solution. Another possible cause is local release fibrinolytic agents (plasminogen and urokinase) from the mucosa of the lower urinary tract. During and immediately after TURP, these agents cause local fibrinolysis and promote bleeding from the raw surfaces of the prostatic gland. The existence of a local fibrinolytic mechanism is supported by the observation that prophylactic administration of ϵ-aminocaproic acid (an antifibrinolytic agent) reduces bleeding from the prostatic bed.

Systemic coagulopathy can also occur during TURP. Contrary to common misconception, the coagulopathy is caused by disseminated intravascular coagulation (DIC), rather than by primary fibrinolysis. Characteristically, the platelet count and fibrinogen blood level are abnormally low. At autopsy, multiple microthrombi are observed in various parts of the body. The high level of fibrin-degradation products found in the blood of these patients is caused by secondary fibrinolysis, which commonly accompanies DIC.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia.* 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1365–1368.

Ljungner H, Bergquist D, Isacson S. Plasminogen activator activity in patients undergoing transvesical and transurethral prostatectomy. *Eur Urol.* 1983;9:24–27.

Malhotra V. Transurethral resection of prostate. *Anesthesiol Clin North America.* 2000;18: 883–897.

Miller RD, Eriksson LI, Fleisher MD, et al. *Miller's Anesthesia.* 7th ed. Philadelphia: Churchill Livingstone; 2010:2119–2123.

Smith RB, Riach P, Kaufman JJ. Epsilon aminocaproic acid and the control of postprostatectomy bleeding: a prospective double blind study. *J Urol.* 1984;131: 1093–1095.

C.29. What triggers disseminated intravascular coagulopathy in patients undergoing TURP? How would you treat it?

Apparently, DIC is triggered during TURP by prostatic particles rich in thromboplastin that enter the bloodstream during surgery. The recommended treatment for DIC is

replacement of blood loss and administration of platelets, cryoprecipitates, and fresh frozen plasma. Heparin administration is controversial.

Malhotra V, ed. *Anesthesia for Renal and Genito-urologic Surgery*. New York: McGraw-Hill; 1996:108.

Malhotra V. Transurethral resection of prostate. *Anesthesiol Clin North America* 2000;18: 883–897.

C.30. What are the causes, signs, symptoms, and treatment of bladder perforation during TURP?

The incidence of bladder perforation during TURP is approximately 1% and stems from trauma by surgical instrumentation, overdistention of the bladder, and, rarely, explosion of traces of hydrogen gas inside the bladder.

An early sign of bladder perforation is a sudden decrease in the return of irrigation solution from the bladder. This sign often goes unnoticed until a significant amount of irrigation solution accumulates in the abdomen, causing abdominal distress. Other clinical signs are hypotension, followed by hypertension and nausea. Reflex-type movements of the limbs have been observed under both general and regional anesthesia. When the perforation is intraperitoneal, symptoms develop faster, and include severe shoulder pain caused by diaphragmatic irritation.

Diagnosis of bladder perforation is confirmed by cystourethrography. Treatment is immediate suprapubic cystotomy.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1365–1368.

Hansen RI, Iverson P. Bladder explosion during uninterrupted transurethral resection of the prostate: a case report and experimental model. *Scand J Urol Nephrol*. 1979;13:211–212.

Malhotra V. Transurethral resection of prostate. *Anesthesiol Clin North America*. 2000;18: 883–897.

C.31. What are the causes, signs, symptoms, and preventive measures for bladder explosion during TURP?

A rare but extremely dangerous complication of TURP is gas explosion inside the bladder during surgery. Various explosive gases, particularly hydrogen, are generated by the cauterization of prostatic or bladder tissue during TURP. The explosion is triggered by the hot metal loop of the resectoscope. After a loud thump, the patient complains of sudden abdominal pain. This is accompanied by an abrupt decline in the return of irrigation solution. The concentration of oxygen in the bladder is usually too low to support combustion or explosion. However, if air is allowed to enter the irrigation system during surgery, oxygen concentration in the bladder will rise and this in turn may trigger an explosion.

Strict precautions should be taken to prevent entry of air into the bladder during TURP. If air is observed in the bladder at the beginning of surgery, it must be evacuated before cauterization starts. The bladder should be emptied regularly in order to avoid accumulation of explosive gases during surgery.

Hansen RI, Iverson P. Bladder explosion during uninterrupted transurethral resection of the prostate: a case report and experimental model. *Scand J Urol Nephrol*. 1979;13:211–212.

C.32. What are the causes of hypotension during TURP?

The more common causes of hypotension during TURP are circulatory overloading with CHF, MI or myocardial ischemia, severe anemia resulting from blood loss, and severe hyponatremia and water intoxication.

D. Postoperative Management

D.1. What is the source of postoperative bacteremia in patients who have undergone TURP? What factors increase the incidence of bacteremia?

The prostatic gland often harbors large amounts of various bacteria. TURP facilitates the entry of these bacteria into the bloodstream, leading to postoperative bacteremia. Also, a preoperative indwelling catheter promotes bacterial growth in the urethra. Approximately 30% of patients undergoing TURP have infected urine preoperatively, and half of them sustain bacteremia postoperatively.

Surgical disruption of the prostatic venous sinuses and excessive hydrostatic pressure of the irrigation solution facilitate the entry of bacteria into the bloodstream.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1365–1368.

Malhotra V. Transurethral resection of prostate. *Anesthesiol Clin North America*. 2000;18: 883–897.

D.2. What are the signs of post-TURP septicemia? What preventive measures are generally recommended?

The signs of septicemia usually appear postoperatively in the postanesthesia care unit. They include fever, chills, low blood pressure, and tachycardia.

Antibiotics administered prophylactically before TURP do not sterilize the urine because they do not easily penetrate the prostatic gland. Nevertheless, the preoperative administration of antibiotics is recommended to render the bloodstream hostile to bacteria. The prophylactic administration of antibiotics in patients undergoing TURP is particularly important because of the grave prognosis of septicemia in these patients.

If sepsis is suspected postoperatively in a patient who has undergone TURP, broad-spectrum antibiotics should be started immediately without waiting for blood culture results.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1365–1368.

Malhotra V. Transurethral resection of prostate. *Anesthesiol Clin North America*. 2000;18: 883–897.

D.3. What bacteria-related cause may possibly lead to sudden postoperative shock in patients who have undergone TURP?

Occasionally, patients who have undergone TURP develop postoperatively a short episode of hypotension, severe chills, and fever. However, these symptoms persist only a few hours, and then the patient recovers uneventfully. The cause of these symptoms is not clear; however, absorption of bacterial endotoxins has been suspected. Experimentally, the administration of bacterial endotoxins in humans induced symptoms similar to those described.

Bennett IL. Pathogenesis of fever. *Bull N Y Acad Med.* 1961;37:440–447.

Malhotra V. Transurethral resection of prostate. *Anesthesiol Clin North America.* 2000;18: 883–897.

D.4. Is postoperative hypothermia a risk factor for myocardial ischemia?

Yes. Unexpected hypothermia is associated with a significantly higher incidence of postoperative myocardial ischemia. Therefore, it is important to maintain normothermia during the perioperative period. (See section D.4 in Chapter 13.)

D.5. How would you diagnose perioperative MI?

An intraoperative MI can be totally silent, or the anesthesiologist may become aware of it by a sudden decrease in blood pressure. This sudden decrease in blood pressure may be accompanied by tachycardia, which is indistinguishable from the hypovolemic hypotension resulting from acute blood loss.

The ECG is a good monitor of the adequacy of coronary circulation. Only the appearance of Q waves more than 0.03 seconds in width is definitively diagnostic of MI. However, the Q waves usually appear postoperatively, not intraoperatively. Postoperative measurements of the myocardial isoenzymes of creatine phosphokinase may confirm the diagnosis. However, cardiac-specific enzyme elevations such as troponin I (cTn I), or troponin T (cTn T) are currently the standard of care for biochemical diagnosis of a perioperative MI because they demonstrate sensitivity and tissue specificity superior to other available biomarkers. (See section D.5 in Chapter 13.)

E. Comparing Monopolar, Bipolar, and Laser TURP

E.1. What differentiates monopolar from bipolar TURP?

Monopolar TURP uses high energy, which allows a fast cutting technique of prostatic tissue with minimal coagulation in the process. The body is the conduit of the energy dispersed from the monopolar electrode to complete the electrical circuit to a large-surface skin grounding pad placed on the patient. It also requires the use of an electrolyte-free bladder irrigating fluid. In bipolar TURP, the electrical circuit is completely contained within the resectoscope. This prevents energy from traveling through the body. Instead, the energy remains confined to the site of prostatic resection and is returned via the second limb of the bipolar resectoscope. It has been suggested that with the bipolar electrode, less bleeding occurs at the prostatic tissue site and normal saline can be used as the bladder irrigating fluid.

Issa MM. Technological advances in transurethral resection of the prostate: bipolar versus monopolar TURP. *J Endourol.* 2008;22:1587–1595.

E.2. Are decreased morbidity and mortality associated more closely with monopolar TURP than with bipolar TURP?

In a meta-analysis that reviewed the safety of monopolar versus bipolar TURP in a small number of TURP patients (1,802), a significant benefit was reported in the bipolar group in overall complication rate, need for transfusion, and the absence of TURP syndrome. Recent randomized controlled trials have confirmed this.

Issa MM. Technological advances in transurethral resection of the prostate: bipolar versus monopolar TURP. *J Endourol*. 2008;22:1587–1595.

Qi Chen, Li Zhang, Qi-Liang Fan, et al. Bipolar transurethral resection in saline vs traditional monopolar resection of the prostate: results of a randomized trial with a 2-year follow-up. *BJU International*. 2010;106(9):1339–1343.

E.3. What differentiates the technologies for laser TURP?

Laser prostatectomy has generated renewed interest among urologists, and it is being used in several centers. It is challenging monopolar TURP as an alternative TURP technique. Holmium yttrium–aluminum–garnet (YAG), photoselective high-powered potassium titanyl phosphate (KTP; also known as the Green Light laser), and Greenlight High Performance System (HPS) lasers are the three most recent systems used in TURP. The yttrium–aluminum–garnet laser wavelength is highly absorbed by water, which limits tissue cutting penetration. The potassium titanyl phosphate and High Performance System lasers have a wavelength absorbed by oxyhemoglobin and blood-rich tissue, which vaporizes a very thin prostatic tissue zone. Both techniques create a coagulation zone during resection, which minimizes bleeding and irrigating fluid absorption. There are five advantages of laser TURP: (1) It uses sterile water or normal saline as the irrigating bladder solution; (2) it minimizes the absorption of irrigating fluid; (3) it minimizes or altogether eliminates TURP syndrome; (4) it produces significantly less bleeding, which allows the procedure to be performed on an anticoagulated patient; and (5) it de-emphasizes regional anesthesia as the preferred anesthetic technique.

Hanson RA, Zornow MH, Conlin MJ, et al. Laser resection of the prostate: implications for anesthesia. *Anesth Analg*. 2007;105:475–479.

Shingleton WB, Farabaugh P, May W. Three-year follow-up of laser prostatectomy versus transurethral resection of the prostate in men with benign prostatic hyperplasia. *Urology*. 2002;60:305–308.

Tan AH, Gilling PJ. Holmium laser prostatectomy: current techniques. *Urology*. 2002;60:152–156.

Wosnitzer MS, Rutman MP. KTP/LBO laser vaporization of the prostate. *Urol Clin North Am*. 2009;36:471–483.

F. Are there preferred anesthetic and preferred surgical TURP techniques for this patient?

This 79-year-old man needing TURP has a history of ICD, MI, and recommendation to avoid interruption of antiplatelet therapy due to cardiac stents. With an anticoagulated patient, regional anesthesia would be avoided. This leaves the choice of general anesthesia with consideration of intra-arterial blood pressure monitoring. The advantages of laser TURP would include minimization of prostatic tissue bleeding and lowering the risk of TURP syndrome.

CHAPTER 25

Kidney Transplant

PANCHALI DHAR, PETER FLEISHUT, AND FUN-SUN F. YAO

A 40-YEAR-OLD MAN

with a 10-year history of type 1 diabetes mellitus and hypertension is scheduled to have a living donor renal transplant. He has been on hemodialysis for 5 years.

A. Medical Disease and Differential Diagnosis

1. What are causes of chronic renal disease that can progress to renal failure?
2. How is kidney disease diagnosed and treated?
3. What are the common clinical manifestations of end-stage renal disease (ESRD)?
4. How should anemia be managed in patients with chronic renal disease?
5. What electrolyte imbalances occur in patients with impaired renal function, and how are they treated?
6. When would you correct the metabolic acidosis? What are the dangers of overzealous correction?
7. Are patients with renal disease at increased risk for cardiovascular disease?
8. What is cardiorenal syndrome, and how is it treated?
9. What are the important aspects of immunosuppressive drugs in kidney transplant?
10. Who are expanded criteria kidney donors?
11. What is a living donor transplant program?
12. What is a paired donor exchange transplant program?
13. Is HIV-positive status a contraindication to renal transplant?
14. What surgical techniques are available for donor nephrectomy?
15. How is a donor kidney preserved prior to transplant?
16. Describe the operative procedure of kidney transplantation.

B. Preoperative Evaluation and Preparation

1. What preoperative workup would you order for a recipient?
2. How are routine medications and immunosuppressive medications managed in the perioperative period?

C. Intraoperative Management

1. What type of anesthetic techniques can be used for renal transplant?
2. Is central venous pressure (CVP) monitoring required for the procedure?
3. Is an arterial line required for the transplant procedure?
4. Is a pulmonary artery catheter required for the transplant procedure?
5. What type of intravenous fluid can be used intraoperatively?
6. How would you conduct the anesthesia induction?
7. Is succinylcholine contraindicated in patients with renal failure?
8. How are the nondepolarizing muscle relaxants affected by renal failure?
9. What unusual situations can prolong neuromuscular blockade?
10. How would you maintain anesthesia during the case? What drugs would you use?
11. What are the effects of inhalation anesthetics on renal blood flow (RBF), glomerular filtration, and urine output?
12. What are the potential nephrotoxic effects of inhalation anesthetics? What are the nephrotoxic metabolites of inhalation anesthetics?
13. How does renal failure affect the pharmacology of opioids?

D. Postoperative Management

1. How is the diagnosis of acute transplant rejection made?
2. What are some side effects of immunosuppressive agents of which anesthesiologists should be aware?
3. What is posttransplant erythrocytosis?

A. Medical Disease and Differential Diagnosis

A.1. What are causes of chronic renal disease that can progress to renal failure?

Chronic kidney disease has many potential causes that differ among the world populations. In developed countries, age, hypertension, cardiovascular disease, diabetes, increased body mass index, and smoking are associated with chronic kidney disease. In the developing world, causes of kidney failure include bacterial infection (tuberculosis in India and the Middle East and streptococcal infection in Africa), viruses (human immunodeficiency virus [HIV] and hepatitis B and C in Africa), and parasites (schistosomiasis in Africa and Latin America, leishmaniasis in Africa and Asia, and malaria in Africa). In parts of the world such as Asia, Africa, and the Middle East, environmental and occupational exposure to lead, cadmium, and mercury damage the kidneys.

The most common etiologies of renal disease in the world leading to kidney transplant are:

- Diabetes, 31%
- Chronic glomerulonephritis, 28%
- Polycystic kidney disease, 12%
- Hypertension, 9%
- Systemic lupus erythromatosus, 3%
- Interstitial nephritis, 3%

James MT, Hemmelgram BR, Tonelli M. Early recognition and prevention of chronic kidney disease. *Lancet*. 2010;375:1296–1309.

Wang Y, Chen X, Song Y, et al. Association between obesity and kidney disease: a systematic review and meta-analysis. *Kidney Int*. 2008;73:19–33.

A.2. How is kidney disease diagnosed and treated?

ESRD is established when glomerular filtration rate (GFR) is less than 15 mL per minute.

The Modification of Diet in Renal Disease (MDRD) formula for estimated GFR is:

$$\text{GFR} = 175 \times (\text{standardized Scr})^{-1,154} \times (\text{age})^{-0.203} \times 0.742 \text{ (if female)}$$
$$\text{or} \times 1.212 \text{ (if black)}$$

where Scr is serum creatinine (milligrams per deciliter).

Dialysis is initiated when GFR reaches 10 mL per minute or less in a patient without diabetes or 15 mL per minute in a patient with diabetes. Patients with uremic symptoms (e.g., anorexia, vomiting, weight loss, pericarditis, pleuritis) or fluid overload should be started on dialysis even if GFR has not reached these levels. Other indications for dialysis in chronic kidney disease include hyperkalemia that causes electrocardiogram (ECG) changes or that is persistent (K^+ >6 mEq/L), heart failure poorly controlled with drugs, and metabolic acidosis that is difficult to control.

Rocco MV, Berns JS. Kidney disease outcome quality initiative in the era of global guidelines. *Am J Kidney Dis*. 2009;54:781–787.

Stevens LA, Coresh J, Greene T, et al. Assessing kidney function: measured and estimated glomerular filtration rate. *N Engl J Med*. 2006;354:2473–2483.

A.3. What are the common clinical manifestations of end-stage renal disease (ESRD)?

The common problems related to ESRD are the following:

- Electrolytes: volume expansion, hyponatremia, hyperkalemia, metabolic acidosis, hyperuricemia, hyperphosphatemia, hypocalcemia
- Gastrointestinal: gastroparesis, nausea, vomiting, pancreatitis
- Cardiovascular: accelerated atherosclerosis, systemic hypertension, left ventricular hypertrophy, congestive heart failure, pulmonary edema, cardiomyopathy, pericarditis, hyperdynamic circulation
- Hematologic: anemia, B- and T-cell dysfunction, qualitative platelet dysfunction, bleeding diathesis
- Musculoskeletal: muscle weakness, uremic osteodystrophy (osteomalacia, osteosclerosis, osteitis fibrosa cystica)
- Neurologic: encephalopathy, loss of memory, seizures, peripheral neuropathy, autonomic dysfunction (postural hypotension), myoclonus, asterixis, dialysis disequilibrium (dehydration, weakness, nausea and vomiting, hypotension, and occasionally seizure and coma)
- Gastrointestinal: uremic gastroenteritis, nausea, vomiting, peptic ulcer disease, gastrointestinal bleeding
- Endocrine: vitamin D deficiency, secondary hyperparathyroidism, carbohydrate intolerance, hypertriglyceridemia

Thomas R, Kanso A, Sedor JR. Chronic kidney disease and its complications. *Primary Care Clin Office Pract*. 2008;35:329–344.

A.4. How should anemia be managed in patients with chronic renal disease?

Anemia is often a consequence of progressive renal insufficiency. The anemia is due to several factors, including chronic blood loss, hemolysis, marrow suppression by uremic factors, and reduced renal production of erythropoietin. The decreased production of erythropoietin is the result of a reduction in functioning renal mass. This manifests as a normochromic normocytic anemia. These patients may have hemoglobin levels of 5 to 7 g per dL corresponding to hematocrits of 15% to 25%.

Additional factors that contribute to anemia are iron and folate deficiency, aluminum toxicity, hemolysis, bone marrow fibrosis due to hyperparathyroidism, chronic infection, and hemoglobinopathies. The body compensates for the decrease in oxygen carrying capacity, with an increase in cardiac output and an increase in red blood cell 2-,3-diphosphoglycerate. The increase in 2,3-diphosphoglycerate shifts the oxygen dissociation curve to the right, improving tissue oxygenation.

Patients can be treated with erythropoiesis-stimulating agents (ESAs) to increase hemoglobin levels. The preponderance of the evidence suggests that although ESAs raise hemoglobin A_1c and improve quality of life, targeting the complete correction of anemia with ESA is inadvisable. If patients with renal failure are returned to a normal hematocrit, they run a higher risk for composite death resulting from stroke, myocardial infarction, congestive heart failure, poorly controlled blood pressure, and thrombotic events. The practice at this time is to maintain a conservative target hemoglobin of 11 to 12 g per dL, but not greater than 13 g per dL with ESA treatment.

Intravenous or oral iron supplements are also used to treat anemia. Other novel agents are under investigation. For example, a continuous erythropoietin receptor activator allows less frequent dosing of an ESA. An intravenous iron nanoparticle (ferumoxytol) can raise hemoglobin more than oral iron.

Morris P, Stuart K. *Kidney Transplantation: Principles and Practice*. 6th ed. Philadelphia: Saunders; 2008.

Novak JE, Szczech LA. Triumph and tragedy: anemia management in chronic kidney disease. *Curr Opin Nephrol Hypertension*. 2008;17:580–588.

A.5. What electrolyte imbalances occur in patients with impaired renal function, and how are they treated?

Chronic renal insufficiency and ESRD are associated with impaired excretion and balance of electrolytes.

Sodium and H_2O balance are closely related. In patients with chronic renal failure, the total body content of sodium and H_2O may be increased. This can be due to glomerular disease promoting sodium retention or excessive ingestion of sodium leading to extracellular fluid expansion. The extracellular fluid expansion contributes to hypertension. Nonanuric patients may be treated with loop diuretics and salt restriction.

The renal mechanisms for conserving sodium and H_2O may also be dysfunctional. If additional fluid loss (vomiting, fever) is imposed, such patients become severely volume depleted. The usual indices of prerenal azotemia (high urine osmolality, low urine sodium, and low fractional excretion of sodium) are not applicable because the kidneys cannot conserve sodium or H_2O. These patients have to be hydrated carefully with normal saline.

Chronic hyperkalemia is usually caused by impaired renal potassium excretion. In patients with ESRD or in transplant recipient, hyperkalemia can be exacerbated by excessive dietary intake, hemolysis, hemorrhage, massive blood transfusion, metabolic acidosis, β-adrenergic blockade, angiotensin-converting enzyme inhibitors, angiotensin

receptor blockers, insulin deficiency or resistance, hyperosmolality, hyperglycemia, rhabdomyolysis, succinylcholine, digoxin overdose, or potassium sparing diuretics.

Metabolic acidosis accompanies hyperkalemia. As a general rule, for every 0.1 unit decrease in blood pH, the potassium level increases approximately 0.6 mEq per L. Treatment of hyperkalemia improves the acidosis as well. Severe hyperkalemia increases cardiac and skeletal muscle excitability. The earliest changes begin with levels above 6.5 mEq per L. The ECG shows peaked T waves, flattened P waves, lengthened PR interval, disappearance of P waves, and a widened QRS complex that can progress to a "sine wave," ventricular asystole or ventricular fibrillation. The correlation between serum potassium and ECG changes is not definite because there may be few ECG abnormalities in the presence of severe hyperkalemia. Muscle weakness can cause respiratory failure. Membrane excitability is in fact more dependent on the rate of increase in potassium than on potassium concentration per se. Treatment involves: (1) antagonizing the cardiac toxic effects and stabilizing the cardiac membrane with intravenous calcium salts; (2) shifting the extracellular fluid potassium into cells by administering glucose, insulin, β-adrenergic agonists (albuterol), and sodium bicarbonate (Table 25.1). Of note, calcium can potentiate digitalis toxicity. In such circumstances, the calcium gluconate should be added to 100 mL of D_5W and infused over 20 to 30 minutes. The anesthesiologist may also institute hyperventilation in mechanically ventilated patients. Loop diuretics can increase potassium elimination (nonanuric). Hemodialysis or peritoneal dialysis is the definitive treatment for patients with chronic renal failure.

Hypermagnesemia can accompany chronic renal failure, especially when the GFR decreases to less than 10 mL per minute.

High blood magnesium levels cause dose-dependent neuromuscular toxicity. Symptoms include diminished deep tendon reflexes, flaccid paralysis that may progress to respiratory failure. An increased sensitivity to depolarizing and nondepolarizing neuromuscular agents is noted. Bradycardia, hypotension, and heart block are due to the calcium channel blocking effects of magnesium. The acute toxicity can be antagonized by intravenous infusion of calcium. Hemodialysis or peritoneal dialysis can normalize blood magnesium levels.

Phosphate retention occurs when the GFR begins to decline. Retained phosphate promotes secondary hyperparathyroidism by lowering ionized plasma calcium levels, decreasing renal formation of calcitriol (1,25 dihydroxyvitamin D), and stimulating parathyroid hormone gene expression.

Ionized and protein bound calcium levels are lower in uremic patients. This is the result of hyperphosphatemia and reduced gastrointestinal absorption secondary to the decreased production of vitamin D.

Table 25.1 Drug Treatment for Hyperkalemia

DRUG	DOSE
Calcium chloride	5 mL of 10% solution IV over 2 min (monitor for bradycardia)
Calcium gluconate	10 mL of 10% solution IV over 2 min (monitor for bradycardia)
Insulin	5–10 units regular insulin with 1–2 amps $D_{50}W$ IV bolus
Sodium bicarbonate	1 mEq/kg slow IV push or continuous drip; not to exceed 50–100 mEq
β-agonists (albuterol)	2.5 mg mixed with 3 mL isotonic saline through nebulizer every 20 min as tolerated
Diuretic (furosemide)	20–40 mg IV push
Magnesium	1–2 g IV over 30–60 sec; repeat every 5–15 min as required or 3–10 mg/min IV infusion

Hamish T, Ross M. Fluid and electrolyte problems in renal dysfunction. *Anaesth Intensive Care Med*. 2009;10;289–292.

A.6. When would you correct the metabolic acidosis? What are the dangers of overzealous correction?

A mild-to-moderate acidosis is commonly noted when the GFR decreases to less than 20% to 25% of normal. The decreased renal mass results in decrease NH_4^+ production and excretion of proton load. The plasma bicarbonate concentration ranges between 12 and 22 mEq per L, and blood pH remains greater than 7.20. This does not routinely require correction. It may gradually evolve into a high anion gap acidosis when the GFR is below 20 mL per minute. Some patients with ESRD maintain close to normal acid–base parameters even when renal function is severely compromised. However, when exposed to an increased dietary acid load, these patients may have decreased ability to increase bicarbonate generation. Chronic acidosis promotes muscle wasting, reduces albumin synthesis, impairs bone formation, and decreases insulin sensitivity. There are no guidelines requiring the correction of acidosis to normal pH. Each case should be treated on an individual basis. The recommendations in regard to the amount of bicarbonate to be administered to the patient with acidosis is based on the space of distribution of bicarbonate, which in metabolic acidosis is 50% of lean body weight, and the maximum desired level of plasma bicarbonate, which is 24 mEq per L. The bicarbonate required can be calculated as follows:

$$HCO_3^- \text{ replacement} = 0.5 \times \text{weight in kg} \times (24 - \text{serum } HCO_3^-)$$

Only half of the calculated bicarbonate is given because doses exceeding 1 mEq/kg/min may lead to alkaline overshoot. Serial blood gases should be followed to monitor the response to treatment. Overzealous use of sodium bicarbonate may cause volume overload, promote metastatic calcification by decreasing the solubility of calcium phosphate, and decrease ionized calcium. For each 0.1 increase in pH, oxygen availability may decrease by 10% because of the shift of the oxygen–hemoglobin dissociation curve to the left. Severe symptomatic acidosis (pH <7.20) that is resistant to bicarbonate administration requires dialysis.

Chiu YW, Mehrotra R. What should define optimal correction of metabolic acidosis in chronic kidney disease? *Semin Dialysis*. 2010;23:411–414.

Fauci AS, Braunwald E, Kasper DL, et al. *Harrison's Principles of Internal Medicine*. 17th ed. New York: McGraw-Hill; 2008:289–90, 1764.

A.7. Are patients with renal disease at increased risk for cardiovascular disease?

Premature cardiovascular disease is a leading cause of death in patients with chronic kidney disease. The prevalence of hypertension, coronary artery disease, congestive heart failure, uremic cardiomyopathy, carotid artery stenosis, and aortic aneurysm is greater in the chronic kidney disease population. The mortality rate from myocardial infarction and after undergoing percutaneous coronary angioplasty, coronary artery bypass surgery, or even insertion of an implantable defibrillator is higher in those with renal disease compared to the general population.

The annual rate of sudden cardiac death of a patient with ESRD receiving dialysis is approximately 7%. In patients receiving dialysis, sudden cardiac death and heart failure—not myocardial infarction—are the prevailing modes of cardiovascular death. This increased risk for sudden death can be attributed to myocardial structural changes. Left ventricular hypertrophy is almost universal in the chronic kidney disease population. The left ventricular mass is correlated with survival. The uremic load results in cardiac fibrosis and in left ventricular systolic and diastolic dysfunction. These myocardial structural changes enhance the electrical irritability of the cardiac muscle.

Accelerated atherosclerosis is promoted by diabetes, dyslipidemias, and a decreased GFR. The enhanced calcification occurs throughout coronary and systemic arteries. Plaque formation in the aorta decreases its compliance and increases cardiac afterload. Intensive lipid lowering with statin medications is advocated.

Hypertension develops in 80% of patients with chronic kidney disease. It is due to volume expansion resulting from salt and water retention. High levels of renin-angiotensin secondary to relative intravascular volume depletion contribute to hypertension. An imbalanced autonomic system results in an exaggerated sympathetic drive with a loss of vagal tone. Autonomic neuropathy creates a setting for silent myocardial ischemia and ventricular tachycardia triggered by QTc interval prolongation.

Cooper HA, Monge C, Panza JA. Patients with ESRD and acute myocardial infarction have poor short term outcomes despite modern cardiac intensive care. *Coronary Artery Dis*. 2008;19:231–235.

Remppis A, Ritz E. Cardiac problems in the dialysis patient: beyond coronary disease. *Semin Dialysis*. 2008;21:319–325.

A.8. What is cardiorenal syndrome, and how is it treated?

Cardiorenal syndrome is disorder of the heart and kidneys in which acute or chronic dysfunction in one organ may induce acute or chronic dysfunction in the other organ.

The five types of cardiorenal syndrome are based on the initial onset of either heart or kidney dysfunction. Treatment modalities involve rapid volume removal with diuretics, hemodialysis, and ultrafiltration.

Type 1 cardiorenal syndrome is an abrupt worsening of cardiac function (e.g., acute cardiogenic shock or decompensated congestive heart failure) leading to acute kidney injury.

Type 2 cardiorenal syndrome involves chronic abnormalities in cardiac function (e.g., chronic congestive heart failure) causing progressive and permanent chronic kidney disease.

Type 3 cardiorenal syndrome consists of an abrupt worsening of renal function (e.g., acute kidney ischemia or glomerulonephritis) causing acute cardiac disorder (e.g., heart failure, arrhythmia, ischemia).

Type 4 cardiorenal syndrome is a state of chronic kidney disease (e.g., chronic glomerular disease) contributing to decreased cardiac function, cardiac hypertrophy, or increased risk for cardiovascular events.

Type 5 cardiorenal syndrome is a systemic condition (e.g., diabetes mellitus, sepsis) causing both cardiac and renal dysfunction.

Ronco C. Cardiorenal syndromes: definition and classification. *Contrib Nephrol*. 2010; 164:33–38.

A.9. What are the important aspects of immunosuppressive drugs in kidney transplant?

In order to decrease the incidence of graft rejection, several regimens of immunosuppressive agents have been devised. Centers throughout the world may use different combinations of these drugs, but the basic idea behind their use is to prevent acute and chronic T-cell alloimmune rejection. The regimens are separated into the induction phase and long-term maintenance phase. Four classes of immunosuppressive medications are used: corticosteroids, calcineurin inhibitors (cyclosporine and tacrolimus), antimetabolites (mycophenolate mofetil, mycophenolate sodium, and azathioprine), and the target-of-rapamycin inhibitor, sirolimus. The maintenance phase involves a combination of two or three of these drugs, each from a separate class

Immunosuppressant therapy is started in the immediate preoperative period. In the intraoperative period, induction therapy is targeted to eliminate lymphoid cells that may cause acute rejection of the graft. An induction agent may be withheld if immediate graft function occurs from a living donor kidney. After surgery, maintenance therapy is begun for the life of the recipient. Although lifelong immunosuppression helps prevent rejection of the allograft, it also increases the risk for malignancy and infectious diseases. The regimens may not prevent the slow deterioration associated with chronic graft rejection.

Corticosteroid-free regimens are increasing being used in some transplant centers. This is because the long-term use of corticosteroids contributes to cardiovascular disease or infectious disease complications. There is a slight initial increase in acute graft rejection without corticosteroids, but selected candidates have fared well.

Cruzado JM, Bestard O, Grinyo JM. New immunosuppressive protocols with the advent of novel biological drugs. *Transplantation*. 2009;88(suppl 3):S20–S23.

Leichtman AB. Balancing efficacy and toxicity in kidney transplant immunosuppression. *N Engl J Med*. 2007;357:2625–2627.

Luan FL, Steffick DE, Ojo AO. Steroid free maintenance immunosuppression in kidney transplantation: is it time to consider it as standard therapy? *Kidney Int*. 2009;76:825–830.

A.10. Who are expanded criteria kidney donors?

There are an increasing number of persons awaiting a kidney transplant. The ideal donor is 5 to 49 years old and nonhypertensive, whose cause of death was not cerebrovascular accident and whose creatinine was 1.5 mg per dL or less. The term "expanded criteria donor" has been introduced as a part of an effort to increase the use of kidneys that might otherwise have been discarded and to minimize the length of cold ischemia to which they are subjected. Expanded criteria donors are defined as donors older than age 60 years or 50 to 59 years with two additional risk factors, including a history of hypertension, death as a result of cardiovascular accident, or serum creatinine 1.5 mg per dL or greater. Expanded criteria donor kidneys account for approximately 15% of deceased donor kidneys, but have at least a 70% increased risk for failure within 2 years compared with standard criteria kidneys. The long-term survival of single or dual kidney grafts from donors older than 60 years is excellent, provided that the grafts are evaluated histologically before implantation. Expanded criteria donor kidneys are offered only to patients willing to accept them. Often, this decision must be made within 2 hours. This has increased the number of transplants. The outcome data from expanded criteria donor programs indicate that patients younger than 40 years or scheduled for kidney retransplantation should not receive an expanded criteria donor kidney. Patients 40 years or older, especially with diabetic nephropathy or nondiabetic disease, but a long expected waiting time for kidney transplantation, show better survival receiving an expanded criteria donor kidney than remaining on dialysis therapy.

Fraser SM, Rajasundaram R, Aldouri A, et al. Acceptable outcome after kidney transplantation using "expanded criteria donor" grafts. *Transplantation*. 2010;89:88–96.

Pascual J, Zamora J, Pirsch JD. A systematic review of kidney transplantation from expanded criteria donors. *Am J Kidney Dis*. 2008;52:553–586.

A.11. What is a living donor transplant program?

A living donor transplant program allows recipient and donor surgery to be scheduled simultaneously. It offers the advantage of minimal organ preservation time. The total ischemia time from removal of the kidney from the donor to the restoration of blood flow in the recipient can be less than 1 hour. A short preservation time allows immediate graft function, high volume urine output, and initiation of creatinine clearance.

A large number of recipients have preformed antibodies to potential living donors. These antibodies are the result of exposure to foreign antigens by blood transfusions, prior transplantation, or pregnancy. As a result, the recipients have positive cross matches against living donor tissue antigens. Preoperative measures can facilitate the transplant. The recipient undergoes several pretransplant plasmapheresis sessions to remove the offending antibodies and receives intravenous immunoglobulin to inhibit the return of antibodies. The living donor transplant is conducted when the cross match converts to negative. The recipient usually has to undergo additional plasmapheresis treatments and immunoglobulin infusions postoperatively.

Magee CC. Transplantation across previously incompatible immunological barriers *Transplant Int*. 2006;19:87–97.

Thielke JJ, West-Thielke PM, Herren HL, et al. Living donor kidney transplantation across positive crossmatch: the University of Illinois at Chicago experience. *Transplantation*. 2009;87:268–273.

A.12. What is a paired donor exchange transplant program?

The paired donor exchange transplant program is sometimes referred to as a "kidney swap." As an example, a pair of living donors may have an incompatible blood type or antigens to their intended recipient. The donors agree to exchange recipients. Each donor gives a kidney to an unknown but compatible individual. As a result, the donors provide two patients with healthy kidneys. Each recipient receives a compatible graft.

A chain of paired kidney donations was done in which the transplantations were initiated in July 2007 by a single altruistic donor (i.e., a donor without a designated recipient) and coordinated over a period of 8 months by two large paired-donation registries. These transplantations involved six transplantation centers in five states. In the case of five of the transplantations, the donors and their co-registered recipients underwent surgery simultaneously. In the other five cases, "bridge donors" continued the chain as long as 5 months after the coregistered recipients in their own pairs had received transplants.

There are many benefits to a paired donor exchange program:

- It expands the pool of donors.
- By using ABO-compatible but nonidentical donors, transplants can be performed at individual centers without requiring large sharing networks.
- Type O recipients with incompatible donors are likely to be the primary beneficiary of exchange programs.
- These programs reflect a paradigm shift for live donation, converting a private resource (the donor) to a shared one.

- Both donors and recipients are more willing to participate if their intended recipient or donor is enthusiastic about participating.

Ratner LE, Rana A, Ratner ER, et al. The altruistic unbalanced paired kidney exchange: proof of concept and survey of potential donor and recipient attitudes. *Transplantation*. 2010;89:15–22.

Rees MA, Kopke JE, Pelletier RP, et al. A non-simultaneous, extended, altruistic donor chain. *N Engl J Med*. 2009;360:1096–1101.

A.13. Is HIV-positive status a contraindication to renal transplant?

Chronic kidney disease now accounts for more than 10% of HIV-related deaths. HIV infection is no longer an absolute contraindication to kidney transplantation. The potential recipient should be clinically stable on highly active antiretroviral therapy (HAART), is RNA-negative, and has a CD4 count of 200 cells per mm^3 or greater. There is a risk for developing opportunistic infections, viremia, and malignancy while under immunosuppressive maintenance. Long-term allograft survival is lower among patients who are HIV-positive.

The diagnosis of AIDS (Centers for Disease Control and Prevention definition of CD4 count less than 200 cells per mm^3) is a contraindication to receiving a kidney.

Locke JE, Montgomery RA, Warren DS, et al. Renal transplant in HIV positive patients: long-term outcomes and risk factors for graft loss. *Arch Surg*. 2009;144:83–86.

Reese PP, Blumberg EA, Bloom RD. Kidney transplantation in patients with HIV infection. *Adv Chronic Kidney Dis*. 2010;17:94–101.

A.14. What surgical techniques are available for donor nephrectomy?

Laparoscopic living-donor nephrectomy has increased in popularity. In some centers, it has replaced open donor nephrectomy as the standard technique.

The robotics system provides considerable potential benefits to minimally invasive surgery compared with standard laparoscopic approaches. In particular, the system restores the three-dimensional vision lost in the laparoscopic approach and enhances the ability of the surgeon to perform complex tasks in a laparoscopic environment.

The standard techniques for donor nephrectomy are open surgery, laparoscopic, and hand-assisted laparoscopic donor nephrectomy. Laparoscopic donor nephrectomy results in less blood loss, reduced operative time, and shorter hospital stay than open donor nephrectomy. Hand-assisted laparoscopic donor nephrectomy has the potential to decrease warm ischemia time for renal allografts. Donors managed laparoscopically had fewer complications, significantly less wound-related morbidity, and less delayed graft function than patients who underwent open donor nephrectomy.

Dolce CJ, Keller JE, Walters KC. Laparoscopic versus open live donor nephrectomy: outcomes analysis of 266 consecutive patients. *Surg Endosc*. 2009;23:1564–1568.

Leventhal JR, Paunescu S, Baker TB, et al. A decade of minimally invasive donation: experience with more than 1200 laparoscopic donor nephrectomies at a single institution. *Clin Transplant*. 2010;24:169–174.

A.15. How is a donor kidney preserved prior to transplant?

Two different methods of organ preservation are used for deceased donor kidneys—static cold storage and hypothermic machine perfusion. In static cold storage, the kidney is flushed, cooled with one of several cold preservation solutions, and transported on ice. In hypothermic machine perfusion, after an initial washout of blood, the kidney is connected to a perfusion device and a solution is pumped continuously through the organ at temperatures between 1° and 10° C until the moment of graft placement.

Preservation solutions are agents that do not readily permeate the cell membrane and have an electrolyte composition similar to the intracellular environment (low sodium, high potassium), thus preventing loss of cellular potassium. The organ-preserving cold storage interval is called cold ischemia time. It extends from the initiation of cold preservation of donor organs to restoration of warm circulation in the organ recipient. There is a significant reduction in the mean cold ischemia time over the last decade, and fewer kidneys are being cold stored longer than 30 hours. The influence of improved immunosuppression, lower cold ischemia time have contributed to the recent improvements in graft function and survival.

Kidneys from living donors maybe flushed with preservation solution or iced lactated Ringer's solution containing heparin and mannitol. The ischemic time during implantation is usually 20 to 30 minutes because the transplant operation takes place immediately. Some practices place the living donor kidney in a pulsatile preservation machine that maintains organ viability for longer periods.

Moers C, Smits JM, Matthius MHJ, et al. Machine perfusion or cold storage in deceased donor kidney transplantation. *N Engl J Med*. 2009;360:7–19.

Salahudeen AK, May W. Reduction in cold ischemia time of renal allografts in the U.S. over the last decade. *Transplant Proc*. 2008;40:1285–1289.

A.16. Describe the operative procedure of kidney transplantation.

Before the induction of anesthesia, a large-bore peripheral intravenous line (18- or 16-gauge) is required. Following induction of anesthesia, a triple-lumen central line may be placed for an internal jugular or subclavian route. A Foley catheter is placed in the bladder, and the bladder is irrigated with an antibiotic solution. Fluids are infused liberally through the central line and intravenous line. An arterial line may also be placed, depending on the patient's underlying clinical status.

A kidney is harvested from a living donor using a left-flank laparoscopic approach. Harvesting of the left kidney is favored because the left renal vein is longer. New surgical techniques allow preservation of longer arterial length on the harvested kidney. Longer vessel preservation facilitates a right kidney donation.

The donor kidney is placed in either the right or left iliac fossa. The right kidney is usually placed in the left groin and vice versa. The renal artery of the donor kidney is connected to the external or internal iliac artery in the recipient. The renal vein of the donor kidney is connected to the external iliac vein in the recipient. Occasionally, a donor kidney has multiple renal arteries. This is addressed using primary or secondary anastomosis. A multiple-artery donor kidney has a longer operative and ischemic time than a kidney with a single artery. In the event that the recipient weighs less than 20 kg, the kidney is placed intra-abdominally posterior to the right colon. Urinary continuity is restored by placing the distal ureter into the bladder through a tunnel without opening the bladder.

In deceased donor kidney transplant, before the release of the arterial clamp and following completion of the anastomosis, an intra-arterial injection of verapamil or papaverine may be given by direct push into the renal artery to prevent arterial vasospasm.

In dual kidney transplantation, two kidneys from a donor are placed into one recipient. Such kidneys have usually been refused for single kidney transplantation. Dual kidney transplant is done at the extremes of donor age. It is a reflection of donor shortage and reluctance to discard potentially functional organs. For donors younger than 2 years of age, both kidneys are transplanted en bloc with the donor aorta, which is then anastomosed to the external iliac artery.

If the donor is 60 years or older, the creatinine clearance should be less than 70 mL per minute. A dual kidney transplant procedure is of longer duration and involves more third spacing, greater volume requirements, and blood loss.

Keller JE, Dolce CJ, Griffin D, et al. Maximizing the donor pool: use of right kidneys and kidneys with multiple arteries for live donor transplantation. *Surg Endosc*. 2009;23: 2327–2331.

Saidi R, Kawai T, Kennealey P, et al. Living donor kidney transplantation with multiple arteries: recent increase in modern era of laparoscopic donor nephrectomy. *Arch Surg*. 2009;144:472–475.

Shapiro R, Sarwal MM. Pediatric kidney transplantation. *Pediatric Clin North Am*. 2010;57: 393–400.

B. Preoperative Evaluation and Preparation

B.1. What preoperative workup would you order for a recipient?

The transplant recipient should have routine systemic tests such as ECG, chest radiograph, blood counts, platelet count, electrolytes, serum glucose, blood urea nitrogen, creatinine concentration, prothrombin time, partial thromboplastin time, liver function enzymes (aspartate aminotransferase [AST], alanine aminotransferase [ALT]), bilirubin, and albumin. Dialysis, if indicated, is done within 24 hours of the operation. It is best to avoid overzealous ultrafiltration because expanded filling pressures are desired. A urinalysis and urine culture should be performed on all urinating patients.

Dialysis-related problems such as dialysis dementia, disequilibrium syndrome after dialysis (cerebral edema), hypovolemia (hypotension after anesthetic induction following recent dialysis), and peritonitis (peritoneal dialysis), systemic anticoagulation (after dialysis) should be evaluated. It is important to know the time of the last dialysis. The dialysis records should be reviewed for predialysis and postdialysis body weight. The loss of more than 2 kg during dialysis suggests intravascular volume depletion, which may result in severe hypotension during or after anesthetic induction.

SarinKapoor H, Kaur R, Kaur H. Anaesthesia for renal transplant surgery. *Acta Anaesthesiol Scand*. 2007;51:1354–1367.

B.2. How are routine medications and immunosuppressive medications managed in the perioperative period?

Patients awaiting transplant often have comorbidities such as hypertension and diabetes. Antihypertensive drugs should be continued until the time of surgery. In spite of continuing antihypertensive therapy, patient hemodynamics remain labile. Approximately 50% to 70% of patients are noted to have exaggerated blood pressure responses to induction, laryngoscopy, intubation, and extubation. Oral hypoglycemic agents should be held on the morning of surgery. An aspart insulin (Novolog) sliding scale can be used to manage patients on insulin. The sliding scale may be used intraoperatively if high blood glucose

levels are measured. Antibiotic prophylaxis for infectious complications include a first-generation cephalosporin (cefazolin 1 g 30 minutes preoperatively) or if penicillin allergic, vancomycin (1 g intravenously).

Anxlioytic agents should be titrated carefully because these patients may have increased sensitivity to premedication drugs. For example, diazepam is highly bound to albumin, but with decreased albumin levels, the effect of the drug is increased. Midazolam is water soluble, less affected by albumin levels, and useful before induction.

Transplant recipients begin their immunosuppressive regimens before entering the operating room. Immunosuppressive medications are administered for an additional 4 days, at which time recipients are typically discharged.

At New York Presbyterian Hospital, a corticosteroid-sparing regimen is usually followed. Approximately 80% of our transplant recipients are judged to be suitable for corticosteroid-free immunosuppression and go home taking only tacrolimus (Prograf) and mycophenolate mofentil (CellCept).

Before entering the operating room, patients are given intravenous methylprednisolone (Solu Medrol), and mycophenolate mofentil (CellCept). Diphenhydramine and acetaminophen are given as prophylaxis before the rabbit antithymocyte globulin (Thymoglobulin) is infused intraoperatively. Under specific circumstances, basiliximab (Simulect) is substituted for Thymoglobulin. This is the case if the patient has history of reaction to thymoglobulin or is a perfect match to the donor kidney. No prophylactic premedication is required with basiliximab. Patients receive only five doses of methylprednisolone; corticosteroids are then discontinued. In the corticosteroid protocol, patients are continued on prednisone. Rituximab and plasmapheresis followed by intravenous immunoglobulin are incorporated into the regimens of those patients with a positive crossmatch.

Morris P, Stuart K. *Kidney Transplantation: Principles and Practice*. 6th ed. Philadelphia: Elsevier; 2008:187–188.

New York Presbyterian Hospital-Cornell Medical Center Kidney Transplantation Protocol 2009. New York: New York Presbyterian Hospital-Cornell Medical Center; 2009.

C. Intraoperative Management

C.1. What type of anesthetic techniques can be used for renal transplant?

General anesthesia is the preferred technique for renal transplantation. The use of epidural or combined spinal epidural anesthesia is controversial. If the decision is made to use regional anesthesia, certain factors should be considered by the anesthesiologist. General anesthesia with epidural anesthesia has been also used in the past.

It is important to note that uremic bleeding tendency combined with the effects of residual heparin given during dialysis increases the risk of hemorrhage into the epidural space. Underlying hepatic disease can also alter platelet function and decrease coagulation factor levels. Studies have not demonstrated higher plasma concentrations of local anesthetic because of hyperdynamic circulation or acid–base changes in renal patients. The duration of surgery is the major determinant of anesthetic technique. Epidural anesthesia has been used successfully in renal transplant surgery. Hypotension has been shown to be one of the most common hemodynamic changes with the use of an epidural anesthesia. Studies have shown no overall difference in mortality or major morbidity between patients randomly assigned to general anesthesia or combined spinal–epidural anesthesia for renal transplantation. The advantages of the combined technique are rapid onset and good muscle relaxation from the subarachnoid block, with the ability to supplement analgesia through the epidural catheter during and after the surgery. With longer operative times, general anesthesia is preferred.

Bhosale G, Shah V. Combined spinal-epidural anesthesia for renal transplantation. *Transplant Proc*. 2008;40:1122–1124.

Brunicardi FC, Andersen DK, Billiar TR, et al. *Schwartz's Principals of Surgery*. 9th ed. New York: McGraw-Hill; 2010:286.

Morris P, Stuart K. *Kidney Transplantation: Principles and Practice*. 6th ed. Philadelphia: Saunders; 2008:187–209.

C.2. Is central venous pressure (CVP) monitoring required for the procedure?

Adequate hydration is an important part of the anesthetic management in renal transplant. Measuring the CVP is not an absolute requirement. External jugular venous pressure has been used as an alternative to CVP monitoring. The CVP or pulmonary artery pressure can be used to guide fluid therapy. Adequate hemodialysis should be performed within 48 hours of surgery. These postdialysis patients have intravascular volume depletion. To decrease the incidence of postoperative acute tubular necrosis, a liberal hydration policy is employed intraoperatively. Hydration guided by CVP monitoring has been shown to maintain stable hemodynamics and promote diuresis. The systolic blood pressure is maintained between 130 and 160 mm Hg, and the CVP is maintained between 12 and 14 mm Hg. Maintaining adequate CVP is especially important in pediatric recipients because reperfusion of an adult-size kidney graft may divert a significant amount of their own blood volume.

CVP may decline 1 to 2 hours after revascularization despite aggressive fluid management in the operating room. The decline in CVP is similar in recipients of both cadaveric and living related donor kidneys. It may decline 25% to 50% below the CVP measured in the operating room at reperfusion of the transplanted kidney. The reason for the decline is not clear but may be multifactorial, such as redistribution of fluids, changes in vascular permeability, or increased nitric oxide levels. This is why postoperative hydration is an essential factor in maintaining renal function. Increased hydration likely works by atrial distention and the subsequent release of atrial natriuretic peptide and increased renal perfusion. The patient should receive an equal amount of fluid replacing the urine output. This approximates to 1 L per hour.

Brunicardi FC, Andersen DK, Billiar TR, et al. *Schwartz's Principals of Surgery*. 9th ed. New York: McGraw-Hill; 2010:286.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:2164–2165.

Othman MM, Ismael AZ, Hammouda GE. The impact of timing of maximal crystalloid hydration on early graft function during kidney transplantation. *Anesth Analg*. 2010; 110:1440–1446.

Trzebicki J, Flakiewicz E, Nowakowski P, et al. Is external jugular venous pressure a good predictor of volume status in kidney graft recipients? *Transplant Proc*. 2009;41: 3033–3035.

C.3. Is an arterial line required for the transplant procedure?

An arterial line is not absolutely required for the transplant procedure, but many transplant surgeons prefer its placement. It should be placed if a patient has an advanced comorbid condition(s) that requires close monitoring of blood pressure or acid–base status. Often, placement of an intra-arterial line is difficult, because many recipients have poor arterial access secondary to diabetes, peripheral vascular disease, arteriovenous fistulas, and shunts. Major swings in blood pressure may occur, with

hypotension (49.6%) being more likely than hypertension (26.8%). Administration of induction drugs and maintenance agents should be titrated carefully. The main utility of instantaneous blood pressure reading is toward the end of the procedure. Hypotension may occur after unclamping of the iliac vessels or from partial systemic absorption of the vasodilator (verapamil or papaverine) injected by the surgeon into the graft vessels.

Miller RD, ed. *Miller's Anesthesia.* 7th ed. Philadelphia: Churchill Livingstone; 2010:2164–2165.

C.4. Is a pulmonary artery catheter required for the transplant procedure?

A pulmonary artery catheter is not routinely placed for kidney transplantation. Patients with severe comorbid conditions, such as symptomatic coronary artery disease, left ventricular dysfunction, congestive heart failure, valvular heart disease, or severe chronic obstructive pulmonary disease, can be monitored precisely with a pulmonary artery catheter. A transesophageal echocardiography can help determine if hypotension is caused by hypovolemia or myocardial dysfunction.

Miller RD, ed. *Miller's Anesthesia.* 7th ed. Philadelphia: Churchill Livingstone; 2010:2164–2165.

C.5. What type of intravenous fluid can be used intraoperatively?

The administration of normal saline and normal saline–based fluids (5% albumin) is the standard of care for fluid management in patients undergoing renal transplant surgery. This practice is primarily based on avoidance of potassium-containing fluids, which can contribute to intraoperative hyperkalemia. One study suggests a higher risk of acidosis when using normal saline solutions versus lactated Ringer's solution. The typical fluid requirement for a 70-kg adult is about 3,000 to 4,000 mL. In addition, 500 mL of 5% albumin is given.

The recipient's blood is usually typed and screened, but blood loss is minimal, so transfusion is unlikely. The anesthesiologist should attempt to maintain a systolic blood pressure range of 130 to 160 mm Hg, CVP between 10 and 14 cm H_2O, and mean pulmonary artery pressure of 18 to 20 mm Hg.

The intravenous administration of adequate volumes of fluid is associated with earlier onset of graft function, lower postoperative serum creatinine, higher postoperative creatinine clearance, reduced incidence of delayed graft function, and improved graft survival.

Khajavi MR, Etezadi F, Moharari RS, et al. Effects of normal saline vs. lactated Ringer's during renal transplantation. *Renal Failure.* 2008;30:535–539.

New York Presbyterian Hospital-Cornell Medical Center Kidney Transplantation Protocol 2009, New York: New York Presbyterian Hospital-Cornell Medical Center; 2009.

C.6. How would you conduct the anesthesia induction?

The circumstances for renal transplant can vary between a scheduled or emergent procedure. Living donor transplants are scheduled surgical cases. Patients receiving cadaver kidneys may learn of the surgical procedure on short notice. Standard anesthesia monitors are required before induction. The central venous line or arterial line is usually placed after induction.

The induction of general anesthesia and intubation of the trachea can be safely accomplished with several of the commonly used drugs. The induction drugs should be given slowly to minimize the chance of drug-induced hypotension. Regardless of blood volume status, these patients often respond to induction of anesthesia as if they were hypovolemic. The sympathetic nervous system response may be attenuated by antihypertensive therapy or diabetic autonomic neuropathy. A blunted sympathetic response impairs compensatory peripheral vasoconstriction. In addition, the central nervous system may exhibit an increased sensitivity to the induction drugs. Low serum protein and albumin levels can increase the level of unbound drug crossing the blood–brain barrier into central nervous system receptors. Uremia can also disrupt the blood–brain barrier. The dose of induction agent may need to be adjusted based on volume status, acidic pH, and comorbidities. Propofol or etomidate can be used in routine circumstances. A reduced induction dose of propofol may be considered because lower plasma protein levels and postdialysis hypovolemia can exaggerate their cardiodepressant effects. Of note, an animal study model has noted reduced ischemia/reperfusion injury with the use of propofol anesthesia. Ketamine pharmacokinetics is not significantly altered by renal disease, but its hypertensive effects make it undesirable in patients with underlying hypertension. Etomidate is well tolerated and preserves hemodynamic stability.

Large fluctuations in blood pressure and heart rate may occur in patients with preexisting hypertension during intubation. Underlying coronary artery disease is a major consideration. Opioids can blunt the response to laryngoscopy. Fentanyl in moderate doses (5 μg per kg can be used, but a small risk for hypotension exists after induction and lack of stimulation). Remifentanil is also effective for heart rate control. A short-acting β-blocker such as esmolol (0.5 to 1 mg per kg) can blunt the response to intubation.

Various neuromuscular blocking agents can be used to facilitate tracheal intubation. Patients with uremia and diabetes may have gastroparesis. Pretreatment with a clear, nonparticulate antacid such as 30 mL of sodium citrate raises gastric pH. A rapid-sequence induction with cricoid pressure using either succinylcholine or rocuronium may be required to prevent reflux and aspiration. Succinylcholine can be used safely because potassium release is not exaggerated in patients with chronic renal failure. If the preoperative potassium is in the high normal range or if there is underlying metabolic acidosis, the additional increase of 0.5 to 1 mEq per L should be considered. When choosing a nondepolarizing agent for maintenance, it is better to use ones that are independent of renal clearance mechanisms (cis-atracurium, atracurium).

Miller RD ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:2164–2165.

Yuzbasioglu MF, Aykas A, Kurutas EB, Sahinkanat T. Protective effects of propofol against ischemia/reperfusion injury in rat kidneys. *Renal Failure*. 2010;32:578–583.

C.7. Is succinylcholine contraindicated in patients with renal failure?

Normally, succinylcholine causes an increase in serum potassium of 0.5 to 1.0 mEq per L within 3 to 5 minutes after intravenous administration and lasts less than 10 to 15 minutes. Succinylcholine can be used safely in patients with chronic renal failure if the potassium concentration is less than 5.5 mEq per L and repeated doses are avoided. Potassium flux after administration of succinylcholine in patients with renal failure does not differ from normal patients. Plasma cholinesterase activity has been reported to be below normal in more than 20% of patients with ESRD whether they are receiving any form of dialysis. Values are rarely so low that they cause a prolonged block.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010: 2114–2115, 2164–2165.

Table 25.2 Pharmacokinetics of Neuromuscular Blocking Agents in Normal versus Anephric Patients

DRUG	RENAL EXCRETION (%)	NORMAL $t_{1/2}$ (min)	ANEPHRIC $t_{1/2}$ (min)
Pancuronium	85	132	258
Rocuronium	10	42	58
Vecuronium	40–50	54	84
Atracurium	10–40	18	24
Cis-atracurium	16	34	No effect
Mivacurium	< 5%	1.8	3.6
Succinylcholine	< 25%	1	1

C.8. How are the nondepolarizing muscle relaxants affected by renal failure?

Table 25.2 notes the commonly used nondepolarizing agents and how they are affected by renal failure. The prolonged duration of action to nondepolarizing agents is primarily due to slow renal clearance. Cis-atracurium mainly undergo Hoffman elimination that is not altered in patients with chronic kidney disease. Renal failure may delay clearance of laudanosine, the principal metabolite of cis-atracurium. Laudanosine does not have effect at the neuromuscular junction, but at high plasma levels may act as a central nervous system stimulant. The long-acting muscle relaxant such as pancuronium is not suitable for use because the kidneys excrete most of the drug and its metabolite. The prolonged effect of a nondepolarizing agent may not be apparent after a single small dose. After a small dose, the termination of action is by redistribution rather than elimination. It is only after a single large dose, repeated dosing, or prolonged infusion that the increased elimination half-life becomes clinically apparent. It has also been shown that there are large differences in pharmacokinetics with patients with renal failure receiving rocuronium. Maintenance doses for patients with decreased renal function should be smaller, and the interval between doses should be increased. Monitoring of neuromuscular blockade with a nerve stimulator is recommended.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:2114–2115.

Staals LM, Snoeck MM, Driessen JJ, et al. Reduced clearance of rocuronium and sugammadex in patients with severe to end-stage renal failure: a pharmacokinetic study. *Br J Anaesth*. 2010;104:31–39.

C.9. What unusual situations can prolong neuromuscular blockade?

Drugs

- *Antibiotics.* The aminoglycosides (e.g., gentamicin) and tetracycline decrease the presynaptic release of acetylcholine by blocking the influx of calcium. Antagonism of antibiotic potentiated neuromuscular blockade by an anticholinesterase drug or calcium is unpredictable. Penicillins and cephalosporins do not have neuromuscular effects.
- *Local anesthetics.* Small doses of local anesthetics enhance neuromuscular blockade, and large doses block neuromuscular transmission. Depending on the dose,

local anesthetics interfere with the prejunctional release of acetylcholine, stabilize postjunctional membranes, and directly depress skeletal muscle.
- *Cardiac antidysrhythmic drugs.* Lidocaine can augment preexisting neuromuscular blockade. Quinidine interferes with the prejuctional release of acetylcholine and potentiates depolarizing and nondepolarizing drugs.
- *Diuretics.* Furosemide 1 mg per kg enhances nondepolarizing agents by inhibiting cyclic adenosine monophosphate (cAMP) production, leading to decreased prejunctional release of acetylcholine. Large doses of furosemide can inhibit phosphodiesterase, increasing cAMP levels leading to antagonism of nondepolarizing drugs.
- *Phenytoin.* Treatment with phenytoin causes resistance to nondepolarizing drugs.
- *Lithium.* This drug can enhance the effects of nondepolarizing and depolarizing drugs.
- *Calcium channel blockers.* Verapamil enhances nondepolarizing agents and may produce difficulty with obtaining adequate reversal.

Electrolytes

- *Potassium.* An acute decrease in potassium levels increases the transmembrane potential, causing hyperpolarization of cell membranes. This leads to resistance to depolarizing drugs and increased sensitivity to nondepolarizing drugs. An acute increase in potassium has the opposite effect by lowering the resting transmembrane potential and partially depolarizing the cell membrane. This increases the effect of depolarizing drugs and opposes the action of nondepolarizing drugs.
- *Magnesium.* Hypermagnesemia enhances nondepolarizing agents by decreasing the prejunctional release of acetylcholine and postjunctional sensitivity to acetylcholine. Phase II block may occur more readily when succinylcholine is administered in the presence of elevated plasma concentrations of magnesium

Acid–Base Imbalance

- Respiratory acidosis enhances d-tubocurarine (d-Tc)- and pancuronium-induced neuromuscular blockade and opposes their reversal with neostigmine.
- The effects of metabolic acidosis and respiratory and metabolic alkalosis are inconsistent.

Temperature

- *Hypothermia*. A decrease in temperature reduces hepatic enzyme activity responsible for metabolizing d-Tc and pancuronium, prolonging drug effect. Hypothermia can have a direct mechanical effect on the muscle, slowing contraction and relaxation and thereby enhancing the block.

Stoelting RK, Hillier SC. *Pharmacology and Physiology in Anesthetic Practice.* 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2006:224–227.

C.10. How would you maintain anesthesia during the case? What drugs would you use?

General anesthesia is the preferred technique for kidney transplantation. Volatile agents, opioids, and a muscle relaxant are required to provide optimal operating conditions.

The choice of inhaled anesthetic includes desflurane and isoflurane. Sevoflurane may be avoided because the metabolism of sevoflurane has been implicated in renal toxicity as a result of production of fluoride and compound A. Desflurane and isoflurane do not have any nephrotoxic potential secondary to fluoride accumulation.

Opioids such as fentanyl, sufentanil, alfentanil, and remifentanil can be used during the procedure. Morphine and meperidine have metabolites that depend on renal clearance and can accumulate. A muscle relaxant that is not dependent on renal clearance such as atracurium, cis-atracurium, and mivacurium can be used.

Hypotension may occur after unclamping the iliac vessels and reperfusion of the graft. It is important to maintain the blood pressure because renal function is critically dependent on adequate perfusion. It is critical that the patient is adequately hydrated throughout surgery in preparation for reperfusion of the graft. Close monitoring of CVP can prevent hypotension. Vasopressors with α-agonist action should be avoided because they can comprise blood flow to the transplanted organ. Additional fluid may be required to maintain blood pressure and replace urine output. Furosemide and mannitol can enhance urine output. Loop diuretics block the Na and K channels in the thin ascending loop of Henle. This prevents reabsorption of electrolytes in this part of the nephron. The high-osmolar fluid prevents reabsorption of water in the distal tubule. A large volume of fluid with high electrolyte content is excreted. Mannitol is freely filtered in the glomerulus, but not reabsorbed. It causes osmotic expansion of urine volume.

The estimated blood loss during the procedure ranges between 200 and 500 mL. In some cases, greater blood loss may require transfusion of packed red cells. Packed red cells should be cytomegalovirus negative. At the end of surgery, patients can be given reversal agents and extubated promptly. Patients are then transferred to the postanesthesia care unit for continued monitoring of urine output and electrolytes.

Miller RD, ed. *Millers's Anesthesia.* 7th ed. Philadelphia: Churchill Livingstone; 2010: 2164–2165.

Morris P, Stuart K. *Kidney Transplantation: Principles and Practice.* 6th ed. Philadelphia: Saunders; 2008:191.

C.11. What are the effects of inhalation anesthetics on renal blood flow (RBF), glomerular filtration, and urine output?

All volatile anesthetics produce a dose-related transient and reversible decrease in RBF, GFR, urine output, and the urinary excretion of sodium. This is primarily in response to a decline in systemic blood pressure and cardiac output. Reduced RBF, loss of renal autoregulation, and neurohumoral and neuroendocrine factors also contribute. Specific differences among the agents on renal function are to be noted. Halothane does not alter autoregulation of RBF and decreases renal vascular resistance and perfusion pressure proportionally. Isoflurane minimally alters RBF with light levels of anesthesia (1 minimum alveolar concentration and significantly decreases renal vascular resistance. As the depth of anesthesia with isoflurane is increased, RBF decreases because of a greater decrease in perfusion pressure than in vascular resistance.

Hines RL, Marschall KE. *Stoelting's Anesthesia and Co-existing Disease.* 5th ed. Philadelphia: Churchill Livingstone; 2008:338.

Miller RD, ed. *Miller's Anesthesia.* 7th ed. Philadelphia: Churchill Livingstone; 2010:2164–2165.

C.12. What are the potential nephrotoxic effects of inhalation anesthetics? What are the nephrotoxic metabolites of inhalation anesthetics?

Fluoride-induced nephrotoxicity is a potential hazard following metabolism of volatile anesthetics. Desflurane (0.02%), isoflurane (0.2%), enflurane (2%), sevoflurane

(2% to 3%), and halothane (12% to 20%), are metabolized in the body (rule of 2). When serum inorganic fluoride reaches 50 to 80 mmol per L, subclinical renal toxicity (laboratory abnormalities) occurs. Clinical nephrotoxicity usually becomes apparent when the serum fluoride level is more than 80 mmol per L. The high-output renal failure is dose related and characterized by vasopressin-resistant polyuria, hypernatremia, serum hyperosmolarity, increased serum urea nitrogen, and inorganic fluoride concentration. Despite the potential for relatively high plasma levels of fluoride after long exposure to newer anesthetics, the minimal amount of sevoflurane and enflurane renal defluorination may explain the relative absence of serious renal concentrating defects with these anesthetics. Although the conventional measurements of renal function (blood urea nitrogen, creatinine) are not altered, evidence shows transient impairment of renal concentrating ability and renal tubular injury in patients receiving sevoflurane or enflurane. Nevertheless, it has not been confirmed whether administration of sevoflurane in patients with pre-existing renal disease could further deteriorate renal function. Fluoride levels after isoflurane and halothane increase by 3 to 5 μM per L and 1 to 2 μM per L, respectively. These agents do not pose a risk for nephrotoxicity. Desflurane is resistant to biodegradation because fluorine is the only halogen in the desflurane molecule. Mean inorganic fluoride concentration after 1 MAC hour exposure to desflurane is less than 1 μmol per L. Prolonged exposure to desflurane (7.0 MAC hours) has been associated with normal renal function in patients without renal disease. Neither desflurane nor isoflurane lead to a deterioration of creatinine clearance in patients with pre-existing renal impairment.

Sodium or barium hydroxide lime absorbents react with sevoflurane, resulting in a by-product called *compound A*. The nephrotoxic potential of compound A has been noted in animals and is inconclusive in human studies. The concentrations that occur in humans are far below the nephrotoxic levels in animals. A fresh gas flow of 1 L per minute or higher is recommended to minimize the accumulation of compound A in the breathing circuit. Low-flow sevoflurane (1 L per minute) has been used on many occasions with no effect on renal function. Carbon dioxide absorbents that contain calcium hydroxide and calcium chloride do not result in compound A formation when exposed to sevoflurane. The U.S. Food and Drug Administration (FDA) recommends the use of sevoflurane with fresh gas flow rates at least 1 L per minute for exposures up to 1 hour and at least 2 L per minute for exposures greater than 1 hour. Nevertheless, it is important to note that other countries have not recommended such limitations on the clinical use of sevoflurane and problems have not been noted.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:438–439, 1356.

Fink EJ, Malan TP Jr, Isner RJ, et al. Renal concentrating function with prolonged sevoflurane or enflurane anesthesia in volunteers. *Anesthesiology*. 1994;80:1019–1025.

Gentz BA, Malan TP Jr. Renal toxicity of sevoflurane: a storm in a teacup? *Drugs*. 2001;61:2155–2162.

Hines RL, Marschall KE. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone; 2008:338.

Litz RJ, Hubler M, Lorenz W, et al. Renal response to desflurane and isoflurane in patients with renal insufficiency. *Anesthesiology*. 2002;97:1133–1136.

C.13. How does renal failure affect the pharmacology of opioids?

The effect of renal failure on individual opioids varies, so one must consider the effect of renal failure on drug metabolites as well as the parent compound.

Morphine is metabolized in the liver to morphine-6-glucuronide (M6G) (10%), morphine-3-glucuronide (M3G) (55%), and normorphine (4%), all of which are

excreted by the kidneys, along with about 10% of the parent compound, in subjects with normal renal function. M6G has been reported to mediate the central nervous system and causes respiratory depression when it accumulates in renal failure. Meperidine is metabolized in the liver to normeperidine, also excreted by the kidneys. Accumulation of this metabolite may lead to excitatory central nervous system effects such as seizures. Fentanyl is metabolized by the liver, with only 7% excreted unchanged in the urine. Fentanyl is suitable for use during surgery and is safe in the short term. Reports have shown the parent compound accumulating during renal failure, but clinical experience is that there are no adverse effects. If being used long term in patients with renal failure, the pharmacodynamics effects should be monitored carefully. The clearance and half-life of sufentanil and alfentanil are not significantly different in patients with reduced renal function. Remifentanil is metabolized by blood and tissue esterases. The principle metabolite of remifentanil (GR90291) is eliminated by the kidney. The reduced renal elimination of this metabolite is not of clinical significance because the potency is 1 in 4,000 of the parent compound. Alfentanil metabolism occurs by inducible cytochrome c enzymes in the liver, making it suitable for renal failure patients.

Miller RD, ed. *Miller's Anesthesia.* 7th ed. Philadelphia: Churchill Livingstone; 2010:2113–2164.

Niscola P, Scaramucci L, Vischini G, et al. The use of major analgesics in patients with renal dysfunction. *Curr Drug Targets.* 2010;11:752–758.

D. Postoperative Management

D.1. How is the diagnosis of acute transplant rejection made?

There are various forms of rejection, for example, hyperacute, accelerated acute, acute, and chronic. Acute rejection is the most common, but less common with immunosuppressive agents. It is usually seen within days to a few months after transplant. The diagnosis is made with a renal biopsy. In patients with prolonged delayed graft function, surveillance biopsies can detect or exclude acute rejection episodes. The process is associated with systemic symptoms such as fever, chills, malaise, and arthralgias. However, with current immunosuppressive drugs, most acute rejection episodes are generally asymptomatic. Laboratory data note a rapid increase in creatinine of 10% to 25% over baseline with or without a decrease in urine output.

Brunicardi FC, Andersen DK, Billiar TR, et al. *Schwartz's Principals of Surgery.* 9th ed. New York: McGraw-Hill; 2010:274.

D.2. What are some side effects of immunosuppressive agents of which anesthesiologists should be aware?

Some of the side effects may be encountered if a posttransplant patient presents for other surgeries and are pertinent to anesthetic care:

- *Calcineurin inhibitors (cyclosporine, tacrolimus).* Nephrotoxicity, hypertension, hyperchloremic acidosis, hyperkalemia, hypomagnesemia, hypocalcemia, glucose intolerance, coarse tremor, dysesthesia, headache, seizure, prolonged QT interval, hypercoagulability, acute microvascular disease (similar to thrombotic thrombocytopenic purpura)
- *Mycophenolate mofentil.* Nausea, vomiting, cytopenia (leukopenia, anemia, thrombocytopenia), leukocytosis

- *Target of rapamycin inhibitors (sirolimus, everolimus).* Mucocutaneous ulceration, hypokalemia, hypomagnesemia, impaired wound healing, interstitial pneumonia, cytopenia
- *Azathioprine.* Cytopenia, hepatitis

Danovitch GM. *Handbook of Kidney Transplantation.* 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2005:72–134.

van Hoof JP, Christiaans MHL, van Duijnhoven, EM. Tacrolimus and posttransplant diabetes mellitus in renal transplantation. *Transplantation.* 2005;79:1465–1469.

D.3. What is posttransplant erythrocytosis?

Posttransplant erythrocytosis is a persistently elevated hematocrit (greater than 51%) after engraftment. This usually occurs 8 to 24 months after engraftment. It occurs in 10% to 15% of graft recipients. Predisposing risk factors are male gender, retention of native kidneys, smoking, transplant renal artery stenosis, adequate erythropoiesis before transplantation, and rejection-free course. The most effective treat for posttransplant erythrocytosis is inactivation of the renin-angiotensin system by an angiotensin-converting enzyme inhibitor.

Vlahakos DV, Marathias KP, Agroyannis B, et al. Posttransplant erythrocytosis. *Kidney Int.* 2003;63:1187–1194.

CHAPTER 26

Robotic-Assisted Laparoscopic Surgery

JUDITH WEINGRAM

A 72-YEAR-OLD MAN

with biopsy-proved carcinoma of the prostate had a prostate-specific antigen (PSA) of 22 ng per mL but negative pelvic computed tomography (CT) and bone scans. He weighed 120 kg. Despite hypertension and a 50 pack-year smoking history, he was vigorous and active. He was scheduled for a robotic-assisted laparoscopic radical prostatectomy.

A. Medical Disease and Differential Diagnosis

1. What is the incidence of carcinoma of the prostate?
2. How is prostate cancer diagnosed?
3. How is prostate cancer treated?
4. Define laparoscopy.
5. Describe the development of robotic-assisted laparoscopy. How does the surgeon control the robot?
6. What are the advantages and disadvantages of laparoscopy?
7. What are the differences in pulmonary function after laparoscopic cholecystectomy compared with open cholecystectomy?
8. What are the contraindications to laparoscopic surgery? Is pregnancy a contraindication to laparoscopic surgery?
9. What other specialties commonly perform laparoscopic or minimally invasive surgery?
10. Why is carbon dioxide (CO_2) the gas of choice for laparoscopy? What are its disadvantages?
11. How much endogenous CO_2 is produced at basal level and at maximal exercise?
12. How much CO_2 is stored in the body? Where is it stored? Of what significance is this to laparoscopy?
13. Describe the diffusion and solubility properties of CO_2 and their significance in laparoscopy.
14. Is CO_2 soluble in water or plasma? Is it soluble in blood? Why?

B. Preoperative Evaluation and Preparation

1. What do you want to know about this patient's history and physical condition that may affect whether or not you clear him for laparoscopic surgery?
2. What factors increase this patient's risk of pulmonary complications?
3. What laboratory tests should be performed preoperatively?
4. What specific information should the patient be given about laparoscopic surgery before obtaining informed consent?
5. What additional procedures should be done before surgery?
6. What are the three major forces that uniquely alter the patient's physiology during laparoscopy?

C. Intraoperative Management

1. What is the anesthetic technique of choice for laparoscopy? Why?
2. Can a laryngeal mask airway (LMA) be used?
3. What anesthetic agents or adjuvant drugs are recommended for laparoscopy? Are any anesthetic agents contraindicated?
4. Should nitrous oxide (N_2O) be used during laparoscopy? What are the pros and cons? Does N_2O cause bowel distention during laparoscopy? Does N_2O cause nausea and vomiting after laparoscopy?
5. Can laparoscopy be performed under local anesthesia or regional anesthesia?
6. What monitors and devices would you apply to the patient? Why?
7. How is the patient to be positioned? What special precautions are required for robotic laparoscopy?
8. How will you ventilate the patient? What are the respiratory and circulatory effects of the Trendelenburg position during laparoscopy?
9. What two techniques are available for initial laparoscopic access to the peritoneal cavity? What anesthetic problems can arise during insufflation?
10. What intravenous (IV) solution and how much fluid volume do you plan to deliver?
11. What is the purpose of the heparinized saline irrigation-suction device used by the surgeon and why should you be concerned with it?
12. Under what circumstances should laparoscopy be converted to laparotomy?
13. What are the arterial to end-tidal CO_2 gradients ($Paco_2$–$PETCO_2$) in the normal awake patient? What is the cause of the gradient? Does the gradient change during laparoscopy? Why?
14. Is an arterial line necessary? Why? Does end-tidal CO_2 tension accurately reflect arterial CO_2 tension? Under what circumstances may the $PETCO_2$ exceed the $Paco_2$? Why?
15. What are the possible causes of hypercarbia?
16. What factors play a role in the unusually rapid and marked elevation of CO_2 that is sometimes seen in laparoscopy?
17. How rapidly does the $Paco_2$ rise in the apneic patient (endogenous CO_2)? How rapidly does the $Paco_2$ rise if 5% CO_2 gas is inhaled (exogenous)? How rapidly can the CO_2 rise during laparoscopy? What factors explain the differences?
18. What are the direct and indirect effects of hypercarbia on the cardiovascular system? How are these effects altered by increased intra-abdominal pressure and patient position?

19. What are the direct and indirect effects of hypercarbia on the respiratory system? How does the Trendelenburg position and the increased intra-abdominal pressure of pneumoperitoneum alter these effects?
20. What are the direct and indirect effects of hypercarbia on the central nervous system?
21. What are the neuroendocrine changes that occur during laparoscopy?
22. What are the direct and indirect effects of laparoscopy on the renal system?
23. What is the effect of hypercarbia and laparoscopy on the bowel and gastrointestinal system?
24. How would you recognize CO_2 embolism during laparoscopy? How does this differ from air embolism? Why should N_2O be discontinued during suspected embolization? Will N_2O increase the size of the CO_2 emboli?
25. What is the mechanism of increase in shunting resulting from embolization?
26. How is gas embolism (CO_2 or air) treated?
27. What are the causes of pneumothorax or pneumomediastinum during laparoscopy? How would you diagnose it? How would you treat it?
28. How would you decide when to extubate?

D. Postoperative Management

1. What are some of the unique complications of laparoscopy?
2. What postoperative orders will you write? When would you remove the Foley catheter and arterial line? Under what circumstances would you order a chest x-ray film?
3. What is the incidence of postoperative nausea and vomiting?

A. Medical Disease and Differential Diagnosis

A.1. What is the incidence of carcinoma of the prostate?

Carcinoma of the prostate is the second most common cause of death from cancer in American men. In 1983, the incidence of carcinoma of the prostate was approximately 75,000 new cases along with 25,000 deaths of old cases. In 2010, the American Cancer Society estimates that the incidence will be 217,730 (or 28% of all new cancers), along with 32,050 deaths (or 11% of all cancer deaths).

This "epidemic" increase in carcinoma of the prostate is believed to result from new methods for early detection rather than from a true rise in incidence of the disease. Undetected microscopic prostate cancer cells are believed to be present in 30% to 40% of men over the age of 50, and in 75% of men over the age of 75, but it is estimated that only approximately 8% of these will become clinically significant. It has been stated that more men die *with* prostate cancer than *from* it. Therefore, it is not yet known whether early detection of subclinical disease, much of which may have remained clinically insignificant, will improve survival.

Carcinoma of the prostate is rare in Asian men, whereas African-American men have about twice the incidence as white American men.

Dugan JA, Bostwick DG, Myers RP, et al. The definition and preoperative prediction of clinically insignificant prostate cancer. *JAMA.* 1996;275:288–294.

Jemal J, Siegel R, Xu J, et al. Cancer Statistics, 2010. *CA Cancer J Clin.* 2010;60(5):277–300.

Potosky AL, Miller BA, Albertsen PC, et al. The role of increasing detection in the rising incidence of prostate cancer. *JAMA.* 1995;273:548–552.

A.2. How is prostate cancer diagnosed?

The most reliable methods for diagnosis include digital rectal examination plus the serum PSA level. Palpation of a tumor or indurated area and finding an elevated PSA should be followed by prostatic needle biopsies, perhaps under transrectal ultrasound guidance.

Oesterling JE. Prostate-specific antigen: improving its ability to diagnose early prostate cancer [Editorial]. *JAMA.* 1992;267:2236–2238.

A.3. How is prostate cancer treated?

Treatment choices vary not just with the stage of the disease but also with the patient's age and life expectancy, associated medical conditions, and lifestyle. In patients with localized disease, treatment choices include "watchful waiting," brachytherapy (in which radioactive seeds are implanted in the prostate gland), external beam radiation, and surgery. Surgical options include open radical prostatectomy, or laparoscopic radical prostatectomy, which can be hand-assisted or robot-assisted.

A patient with nonlocalized disease can choose to be treated with radiation, hormones, chemotherapy, or other nonsurgical options, or even to have no treatment.

D'Alonzo RC, Gan TJ, Moul JW, et al. A retrospective comparison of anesthetic management of robot-assisted laparoscopic prostatectomy versus radical retropubic prostatectomy. *J Clin Anesth.* 2009;21(5):322–328.

Menon N, Shrivastava A, Tewari A. Laparoscopic radical prostatectomy: conventional and robotic. *Urology.* 2005;66(5):101–104.

A.4. Define laparoscopy.

Laparoscopy (or peritoneoscopy) is a "minimally invasive" procedure allowing endoscopic access to the peritoneal cavity after insufflation of a gas (CO_2) to create space between the anterior abdominal wall and the viscera. The space is necessary for the safe manipulation of instruments and organs. Laparoscopic surgery can also be extraperitoneal. It can also be gasless with abdominal wall retraction, and, more recently, it may be hand-assisted or robotically assisted.

Seifman BD, Wolf JS. Technical advances in laparoscopy: hand assistance, retractors, and the pneumodissector. *J Endourol.* 2000;14:921–928.

Weingram J. Laparoscopic and laser surgery. In: Malhotra V, ed. *Anesthesia for Renal and Genito-urologic Surgery*. New York: McGraw-Hill; 1996:151–176.

A.5. Describe the development of robotic-assisted laparoscopy. How does the surgeon control the robot?

The era of open incisions in which surgeons could directly see, touch, and manipulate organs was superceded by the era of minimally invasive surgery in which tiny cameras and laparoscopes could be inserted through small ports in the patient's body. However, this technique of conventional laparoscopy is limited by poor depth perception (visualization on a two-dimensional monitor) and the use of long, straight instruments, which limit mobility and dexterity.

Robotic devices were initially designed by NASA for the purpose of performing tasks outside the Space Shuttle while being controlled remotely from inside the spacecraft or from earth. This technology was adapted for surgery as the DaVinci computer-assisted robotic system.

The surgeon sits at a remote control console near the patient and operating room table and views the operative field as a high-resolution magnified three-dimensional image transmitted by the video camera. By using two hand-and-finger control devices, the surgeon can precisely manipulate the two mechanical arms of the robot. Foot pedals also allow the surgeon to more precisely control the robot, camera, and cautery.

Wilson T, Torrey R. Open versus robotic-assisted radical prostatectomy: which is better? *Curr Opin Urol.* 2011;21(3):200–205.

Berryhill R, Jhaveri J, Yadav R, et al. Robotic prostatectomy: a review of outcomes compared with laparoscopic and open approaches. *Urology.* 2008;72(1):15–23.

A.6. What are the advantages and disadvantages of laparoscopy?

The advantages include the cosmetic results of small, non–muscle-splitting incisions, decreased blood loss, less postoperative pain and ileus, shorter hospitalization and convalescence, and ultimately lower cost. Postoperative respiratory muscle function returns to normal more quickly than in open surgery, especially in laparoscopic cholecystectomy and other upper abdominal procedures. Wound complications such as infection and dehiscence are less frequent, and host defense mechanisms may be greater in laparoscopic than in open surgery.

The disadvantages include the long learning curve for the surgeon (most complications occur during the first 10 laparoscopies), the narrowed two-dimensional visual field on video in conventional laparoscopy, the need for general anesthesia, and the often longer duration. Ideally, surgeons should have more advanced laparoscopic skills, especially in knot tying, suturing, and working two instruments simultaneously. The use of simulators to enhance these skills has been advocated.

Robotic-assisted laparoscopy, by virtue of its better visualization and greater precision, offers greater likelihood of nerve sparing and, therefore, retention of continence and potency. The disadvantages of the robot include the high cost (in millions of dollars) of purchase and maintenance, and the need for a permanently dedicated operating room location for this heavy and bulky equipment.

Collet D, Vitale GC, Reynolds M, et al. Peritoneal host defenses are less impaired by laparoscopy than by open operation. *Surg Endosc.* 1995;9:1059–1064.

Conacher ID, Soomro NA, Rix D. Anaesthesia for laparoscopic urological surgery. *Br J Anaesth.* 2004;93(6):859–864.

A.7. What are the differences in pulmonary function after laparoscopic cholecystectomy compared with open cholecystectomy?

Pulmonary function is substantially impaired after a large upper abdominal or subcostal muscle-splitting incision, as in open cholecystectomy. Marked diaphragmatic dysfunction occurs postoperatively, caused by both reflex diaphragmatic changes and incisional pain. Vital capacity and functional residual capacity (FRC) may be reduced by 20% to 40% of preoperative values, and they may not return to normal until 2 to 3 days after surgery. The mini incision of laparoscopic cholecystectomy results in far less pulmonary and diaphragmatic loss of function as well as less ileus.

Bablekos GD, Michaelides SA, Roussou T, et al. Changes in breathing control and mechanics after laparoscopic vs open cholecystectomy. *Arch Surg.* 2006;141(1):16–22.

Cunningham AJ, Brull SJ. Laparoscopic cholecystectomy: anesthetic implications [Review]. *Anesth Analg.* 1993;76:1120–1133.

Gunnarsson L, Lindberg P, Tokics L, et al. Lung function after open versus laparoscopic cholecystectomy. *Acta Anaesthesiol Scand.* 1995;39:302–306.

Hong SJ, Cho EJ, Lee JY, et al. The physiologic response to laparoscopic cholecystectomy: CO(2) pneumoperitoneum vs wall lift. *Can J Anaesth.* 2003;50(2):200–201.

Koivusalo AM, Lindgren L. Effects of carbon dioxide pneumoperitoneum for laparoscopic cholecystectomy. *Acta Anaesthesiol Scand.* 2000;44(7):834–841.

Rovina N, Bouros D, Tzanakis N, et al. Effects of laparoscopic cholecystectomy on global respiratory muscle strength. *Am J Respir Crit Care Med.* 1996;153:458–461.

A.8. What are the contraindications to laparoscopic surgery? Is pregnancy a contraindication to laparoscopic surgery?

Increasing experience with the laparoscopic technique has made most contraindications relative rather than absolute. However, it is probably best to avoid or to use extreme caution in patients with coagulopathy, diaphragmatic hernia, severe cardiovascular or pulmonary disease (including bullae), increased intracranial pressure or space-occupying masses, retinal detachment, impending renal shutdown, a history of extensive surgery or adhesions, sickle cell disease (because sickle crisis may be precipitated by acidosis), peritonitis, a large intra-abdominal mass, tumor of the abdominal wall, or hypovolemic shock. Patients with shunts (e.g., ventriculoperitoneal) are at risk for gas emboli, shunt obstruction, and intracranial hypertension, all of which may occur during laparoscopy and may require intracranial pressure monitoring and ventricular drainage if laparoscopic surgery is necessary. In summary, most of the contraindications concern patients who are unable to tolerate extremes of position, pneumoperitoneum, and/or hypercarbia.

Although pregnancy has been considered a contraindication to laparoscopic surgery in the past, an increasing number of such procedures are being performed in the parturient. Laparoscopic cholecystectomy is now more frequent than open cholecystectomy in the pregnant patient. The overall objective of laparoscopic and open surgery is to preserve fetal and maternal well-being and to prevent premature labor. In addition to the general problems of anesthesia for the parturient, the anesthesiologist also must consider the specific problems that result from the interplay between the anatomic and physiologic changes of pregnancy and the anatomic and physiologic triad of pneumoperitoneum, hypercarbia, and positional changes.

Factors to consider in the management of the pregnant patient include awareness of her increased blood volume, increased cardiac output, decreased systemic vascular resistance (SVR), hypercoagulability, the supine hypotensive syndrome, increased respiratory minute volume, decreased residual volume, decreased FRC, increased oxygen consumption, mild hypocapnia, increased risk of aspiration, and decreased anesthetic requirement.

This combination of factors tends to promote hypercarbia and hypoxemia. However, extreme hyperventilation may result in decreased uteroplacental perfusion. Arterial blood gas monitoring has been suggested to detect fetal acidosis because capnography may not reveal a large arterial to end-tidal difference in CO_2. In all cases, preoperative and postoperative fetal and uterine monitoring is essential.

Chohan L, Kilpatrick CC. Laparoscopy in pregnancy: a literature review. *Clin Obstet Gynecol.* 2009;52(4):557–569.

Cunningham AJ, Schlanger M. Intraoperative hypoxemia complicating laparoscopic cholecystectomy in a patient with sickle hemoglobinopathy. *Anesth Analg.* 1992;75:838–843.

Lachman E, Schienfeld A, Voss E, et al. Pregnancy and laparoscopic surgery. *J Am Assoc Gynecol Laparosc.* 1999;6:347–351.

Ravaoherisoa J, Meyer P, Afriat R, et al. Laparoscopic surgery in a patient with ventriculoperitoneal shunt: monitoring of shunt function with transcranial Doppler. *Br J Anaesth.* 2004;92(3):434–437.

Rosen MA. Management of anesthesia for the pregnant surgical patient. *Anesthesiology.* 1999;91:1159–1163.

Shankar KB, Mushlin PS. Arterial to end-tidal gradients in pregnant subjects. *Anesthesiology.* 1997;87:1596–1598.

Society of Gastrointestinal Endoscopic Surgeons. Guidelines for laparoscopic surgery during pregnancy. Society of Gastrointestinal Endoscopic Surgeons. *Surg Endosc.* 1998;12:189–190.

Steinbrook RA, Bhavani-Shankar K. Hemodynamics during laparoscopic surgery in pregnancy. *Anesth Analg.* 2001;93:1570–1571.

Uzzo RG, Bilsky M, Mininberg DT, et al. Laparoscopic surgery in children with ventriculoperitoneal shunts: effect of pneumoperitoneum on intracranial pressure—preliminary experience. *Urology.* 1997;49:753–757.

A.9. What other specialties commonly perform laparoscopic or minimally invasive surgery?

Laparoscopic procedures in urology have become standard, especially for prostatectomy, uncomplicated adrenalectomy, and nephrectomy, including live donor nephrectomy. Laparoscopic gynecologic surgery includes tubal surgery (sterilization, treatment of ectopic pregnancy, etc.), cystectomies, hysterectomies, various ablations (endometriosis), and so on. Laparoscopy is performed in pregnancy and also in pediatrics. Complications include bladder and ureteral injuries and fistulae, but apparently these are not more prevalent than in standard surgery.

Laparoscopic general surgery includes cholecystectomy, hernia repair, antireflux procedures, splenectomy, appendectomy, bowel surgery including bariatric procedures, and various other upper and lower abdominal procedures.

Thoracoscopic surgery and neurosurgical intracranial surgery using modified laparoscopic instruments, but without the need for gas insufflation, are two of the more recent areas of minimally invasive surgery. Lumbar discectomies and other types of spinal surgery also have been done laparoscopically through an anterior approach. Even autopsies have been attempted laparoscopically. The list continues to grow.

Brown SL, Biehl TR, Rawlins MC, et al. Laparoscopic live donor nephrectomy: a comparison with the conventional open approach. *J Urol.* 2001;165:766–769.

Mage G, Masson FM, Canis M, et al. Laparoscopic hysterectomy. *Curr Opin Obstet Gynecol.* 1995;7:283–289.

Pennant JH. Anesthesia for laparoscopy in the pediatric patient. *Anesthesiol Clin North America.* 2001;19(1):69–88.

Zelko JR, Misko J, Swanstrom L, et al. Laparoscopic lumbar discectomy. *Am J Surg.* 1995;169:496–498.

A.10. Why is carbon dioxide (CO_2) the gas of choice for laparoscopy? What are its disadvantages?

CO_2 is the insufflating gas of choice because it is nonflammable, does not support combustion, readily diffuses across membranes, is rapidly removed in the lungs, and is highly soluble because of rapid buffering in whole blood. The risk of CO_2 emboliza-

tion is small. As much as 200 mL of CO_2 injected directly into a peripheral vein may not be lethal, whereas only 20 mL of air may prove to be so. In addition, CO_2 levels in blood and expired air can easily be measured, and its elimination can be augmented by increasing ventilation. As long as oxygen requirements are met, a high concentration of blood CO_2 can be tolerated. Also, medical grade CO_2 is readily available and inexpensive.

It is for these reasons that the following gases are unsatisfactory for pneumoperitoneum: nitrous oxide (does not cause pain intra-abdominally but does not suppress combustion); oxygen (flammable); helium; air and nitrogen (each has no hemodynamic or acid-base sequelae, but can cause gas emboli); and argon (adverse effect on hepatic blood flow, emboli).

It should be emphasized, however, that CO_2 plays a duel role in the body, and it is not inert. Under normal circumstances it is an intrinsic waste product of metabolism. Under the circumstances of laparoscopies, it acts as an extrinsic drug often present in quantities far larger than the body is physiologically capable of generating from even the most extreme exercise or hypermetabolic state.

The disadvantages mainly stem from the fact that CO_2 is not inert, and it has contradictory roles as an endogenous chemical and as an exogenous foreign substance. Changes in its concentration and tensions have enormous biochemical and physiologic consequences. Changes at the local tissue level are often at odds with the overall systemic effect. It causes direct peritoneal irritation and pain during laparoscopy under local anesthesia because it transiently forms carbonic acid when in contact with the moist peritoneum. In addition, CO_2 is not very soluble in the absence of red blood cells, and, therefore, it can remain in gaseous form intraperitoneally (subhepatic) after laparoscopy, causing referred shoulder pain. Hypercarbia and respiratory acidosis occur when the buffering capacity of blood is temporarily exceeded. In addition, CO_2 exerts widespread local and (often contradictory) systemic effects that may manifest overall as hypertension, tachycardia, cerebral vasodilation, hypercarbia, and respiratory acidosis.

Menes T, Spivak H. Laparoscopy: searching for the proper insufflation gas. *Surg Endosc.* 2000;14(11):1050–1056.

Tsereteli Z, Terry ML, Bowers SP, et al. Prospective randomized clinical trial comparing nitrous oxide and carbon dioxide pneumoperitoneum for laparoscopic surgery. *J Am Coll Surg.* 2002;195(2):173–180.

Weingram J. Laparoscopic and laser surgery. In: Malhotra V, ed. *Anesthesia for Renal and Genito-urologic Surgery.* New York: McGraw-Hill; 1996:157.

A.11. How much endogenous CO_2 is produced at basal level and at maximal exercise?

CO_2 and water are the major end products of aerobic metabolism in the mitochondria of the cells. Carbonic acid, the major acid produced in the body, is uniquely volatile, and, therefore, it must be largely eliminated by the lungs. (Other acids are eliminated by the kidney.)

At basal rate, an average adult manufactures approximately 200 mL of CO_2 per minute (while consuming 250 mL of O_2) or 12 L of CO_2 (35 g) per hour. At maximal metabolic rate, it is estimated that the body can produce, transport, and excrete 90 to 100 L per hour, an increase of 800% over basal rate.

Kinney JM. Transport of carbon dioxide in the blood. *Anesthesiology.* 1960;21:615–619.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 6th ed. Philadelphia: Butterworth-Heinemann; 2005:148–154.

A.12. How much CO_2 is stored in the body? Where is it stored? Of what significance is this to laparoscopy?

The body contains approximately 120 L of stored CO_2, most of it in the form of carbonate ion in bone. (This is approximately 100 times the amount of stored oxygen.) CO_2 in the blood is in equilibrium with CO_2 in different tissues. The rate of uptake and distribution of CO_2 from the blood (where it exists as bicarbonate ion) depends on the perfusion and storage capacity of those different tissues. The well-perfused tissues, including brain, kidneys, and blood come to rapid equilibrium. The medium-perfused compartment consists mainly of resting skeletal muscle. The slowly perfused compartment, mainly fat and bone (where it exists as the carbonate ion), has the largest CO_2 storage capacity. In contrast to rapidly changing oxygen levels, CO_2 levels reach equilibrium more slowly.

These storage sites serve to buffer and stabilize blood CO_2 levels because they provide a place for excess CO_2 to "park" until ventilation can catch up and restore equilibrium. The increase in CO_2 storage during laparoscopy is illustrated clinically by the decelerating rate of rise in $P_{ET}CO_2$ despite continuing insufflation. Blood or end-tidal CO_2 levels increase rapidly at first, then plateau at between 15 and 35 minutes, despite continuing low flow insufflation. At constant ventilation, CO_2 levels increase, but not as much as if no simultaneous storage processes were occurring. But if ventilation is increased to keep CO_2 constant, then the increase needed is only approximately 40% of the predicted volume of ventilation because of the drain off of CO_2 into the storage sites.

Farhi LE, Rahn H. Dynamics of changes in carbon dioxide stores. *Anesthesiology*. 1960;21: 604–614.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 6th ed. Philadelphia: Butterworth-Heinemann; 2005:158.

Seed RF, Shakespeare TF, Muldoon MJ. Carbon dioxide homeostasis during anaesthesia for laparoscopy. *Anaesthesia*. 1970;25:223–231.

A.13. Describe the diffusion and solubility properties of CO_2 and their significance in laparoscopy.

Diffusion describes the process by which gases travel from an area of higher partial pressure to one of lower partial pressure. For a gaseous environment, Graham's law states that the rate of diffusion of a gas is inversely proportional to the square root of its density (i.e., the smaller the molecule, the more easily it will diffuse).

When that same gas molecule arrives at an aqueous membrane (e.g., a gas–liquid interface), the solubility of that gas in water now becomes the major factor in determining its diffusing capacity (as shown in Table 26.1). The water solubility of CO_2 is

Table 26.1 Influence of Physical Properties on the Diffusion of Gas through a Gas/Liquid Interface

GAS	MOLECULAR WEIGHT	DENSITY RELATIVE TO O_2	SOLUBILITY RELATIVE TO O_2	WATER DIFFUSION CAPACITY RELATIVE TO O_2
O_2	32	1.0	1.0	1.0
N_2	28	0.88	0.515	0.55
CO_2	44	1.37	24.0	20.5
N_2O	44	1.37	16.3	14.0
He	4	0.125	0.37	1.05

24 times that of O_2, whereas the diffusion capacity of CO_2 is 20.5 times that of O_2. The capacity of a gas to diffuse across a membrane is directly proportional to its solubility in water and inversely proportional to its molecular weight. However, the actual movement of that gas across the aqueous membrane depends not only on its diffusing capacity, but more importantly, on the pressure gradient across that membrane.

The fate of CO_2 gas insufflated into the peritoneal cavity is the same that would occur in any other closed but distensible cavity. The pressure obtained within the cavity varies directly with the volume of gas insufflated and indirectly with the compliance of the closed cavity.

Therefore, the ability of CO_2 to move from the closed peritoneal cavity to the lungs for excretion is dependent on its intrinsic diffusion and solubility properties, the rate of continuing CO_2 insufflation, the surface area of the cavity, and the partial pressure difference across membranes.

Lumb AB. *Nunn's Applied Respiratory Physiology*, 6th ed. Philadelphia, PA: Butterworth-Heinemann; 2005:148–152.

McHoney M, Corizia L, Eaton S, et al. Carbon dioxide elimination during laparoscopy in children is age dependent. *J Pediatr Surg*. 2003;38(1):105–110.

A.14. Is CO_2 soluble in water or plasma? Is it soluble in blood? Why?

CO_2 is relatively insoluble in plasma, interstitial fluid, and water. (Think of the rapid escape of gas from a freshly-opened carbonated soft-drink.) The solubility of CO_2 in water at 37° C (98.6° F) is only 0.03 mmol/L/mm Hg. This must be contrasted to the very high solubility of CO_2 in whole blood. This extremely important distinction exists because of a zinc-containing enzyme, carbonic anhydrase, that exists within the erythrocyte but not at all in plasma.

$$H_2O + CO_2 \xrightarrow{\text{carbonic anhydrase}} H_2CO_3 \rightarrow H^+ + HCO_3^-$$

In the equation shown, carbonic anhydrase catalyzes the left side of the equation (i.e., the hydration of CO_2 to H_2CO_3). Once formed, carbonic acid is unstable and immediately dissociates into H^+ and HCO_3^-. It is estimated that without carbonic anhydrase it would take 200 seconds at 38° C (100.4° F) for the previous reaction to come to 10% equilibrium. Because blood travels through the pulmonary capillaries in less than 1 second, carbonic anhydrase speeds up the reaction by a factor of 7,500 times.

Carbonic anhydrase, therefore, allows the insufflated CO_2 gas to be dissolved and carried as bicarbonate in the blood. The process is reversed in the lungs, and the reconstituted CO_2 gas is removed by respiration.

Christian G, Greene NM. Blood carbonic anhydrase activity in anesthetized man. *Anesthesiology*. 1962;23:179–186.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 6th ed. Philadelphia: Butterworth-Heinemann; 2005:148–158.

B. Preoperative Evaluation and Preparation

B.1. What do you want to know about this patient's history and physical condition that may affect whether or not you clear him for laparoscopic surgery?

Because of his advanced age, it is best to form one's own observations of his mental and physical condition. Is he confused, short of breath, kyphoscoliotic, and so forth?

A glimpse at where and how this patient's body weight is distributed means more than just knowing that he weighs 120 kg. Ask about smoking, wheezing, or any change in exercise tolerance, cough, or recent upper respiratory infection. Perform your usual preoperative evaluation and obtain any consultations, which may be informative. Consult with the surgeon regarding the need for appropriate preoperative antibiotics.

Efron DT, Bender JS. Laparoscopic surgery in older adults. *J Am Geriatr Soc.* 2001;49: 658–663.

B.2. What factors increase this patient's risk of pulmonary complications?

- *The laparoscopic procedure itself*. The basic laparoscopic Trendelenburg position and the increased intraperitoneal volumes and pressures in a paralyzed, mechanically ventilated patient cause respiratory dysfunction. Insufflation pressures should not exceed 12 to 15 mm Hg. Lower pressures are especially advantageous in American Society of Anesthesiologists (ASA) class III and IV patients with diminished cardiopulmonary reserve. In addition, an increased CO_2 load might call for respiratory minute volumes that are so large that further cardiopulmonary compromise occurs.
- *Age*. Pulmonary function declines with age, especially in a patient older than age 70.
- *Smoking/chronic obstructive pulmonary disease (COPD)*. Smokers have increased tracheobronchial secretions with decreased ciliary transport function. They may already have significant pulmonary dysfunction, which may be manifested by diminished exercise tolerance. The forced vital capacity may be diminished in restrictive pulmonary disease, whereas the forced expired volume in 1 second is likely to be decreased in obstructive pulmonary disease.
- *Obesity*. Obesity compounds the problems of increased intra-abdominal pressure in the Trendelenburg position. Excessive weight and pressure on the diaphragm and lung bases can lead to marked ventilation and perfusion abnormalities, difficulty in inserting trocars, upward displacement of the carina (leading to possible endobronchial intubation), barotrauma, and so forth.
- *Overhydration*. Patients often experience oliguria during laparoscopy. This may be interpreted as insufficient hydration, and a relative overtransfusion may ensue. Unless frank pulmonary edema occurs, this cause of mild or moderate respiratory distress in the postanesthesia care unit (PACU) may not be recognized without a chest x-ray film.

Kendell AP, Bhatt S, Oh TE. Pulmonary consequences of carbon dioxide insufflation for laparoscopic cholecystectomies. *Anaesthesia.* 1995;50:286–289.

B.3. What laboratory tests should be performed preoperatively?

Basic tests should include complete blood count, urinalysis, clotting functions, electrocardiogram (ECG), and blood typing and screening. In addition, baseline electrolytes, chemistries, and renal function tests (blood urea nitrogen, creatinine) should be obtained because of the possibility of oliguria during a long laparoscopy. Baseline pulmonary function tests, arterial blood gas measurement, and oxygen saturation values while breathing room air would be helpful in this patient. Markedly abnormal values might suggest the need for bronchodilators, antibiotics, postural drainage, and delay in surgery until pulmonary function is optimal for this particular patient. Baseline chest films are necessary not only to rule out active disease but also for postoperative comparison of acute changes such as subcutaneous or mediastinal emphysema, pneumothorax, or interstitial or pulmonary edema. The presence of

bullae on preoperative chest x-ray films may represent a contraindication to laparoscopic surgery because of the accompanying large tidal volumes and high intrathoracic pressures.

In patients with cardiac issues, echocardiogram, stress test, and cardiology clearance may be advisable.

Miller RD, ed. Millere's *Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:1001–1052.

B.4. What specific information should the patient be given about laparoscopic surgery before obtaining informed consent?

In addition to the usual general complications of the planned surgery and anesthesia, the patient must also be told of the complications unique to laparoscopy, and consent for possible laparotomy must be obtained. Emergency laparotomy may be required in the event of such complications as hemorrhage or organ perforation or because of anatomic or technical reasons. The patient should also be advised of the possibility of postoperative referred shoulder pain.

B.5. What additional procedures should be done before surgery?

Although the surgery is described as minimally invasive, the patient must be ready for maximally invasive surgery if necessary. Therefore, the patient must comply with preoperative orders regarding:

- Diet—it should consist of clear liquids the day before surgery. Nothing orally after midnight.
- A complete bowel preparation is necessary.
- Preoperative antibiotics, as per surgeon.

B.6. What are the three major forces that uniquely alter the patient's physiology during laparoscopy?

- *Pneumoperitoneum*, and problems related to the creation, maintenance, and consequences of the increase in intra-abdominal pressure and volume.
- *Carbon dioxide*, including its chemical and physical properties, and its local and systemic effects.
- Extremes of patient *positioning* on the operating table, which in this case will be steep Trendelenburg.

It is vital that the anesthesiologist have a thorough understanding of the physiologic consequences of changes in these three forces. Separately or in combination, they have profound effects on the patient's hemodynamic, respiratory, and metabolic functions. The early gynecologic laparoscopies were usually brief, and they were performed on young healthy women who tolerated these physiologic trespasses with nearly insignificant changes. These same three forces, however, may produce significant physiologic changes in long, complex laparoscopies in older, sicker patients who may be unable to compensate.

Henny CP, Hofland J. Laparoscopic surgery: pitfalls due to anesthesia, positioning, and pneumoperitoneum. *Surg Endosc*. 2005;19(9):1163–1171.

Hirvonen EA, Poikolainen EO, Paakkonen ME, et al. The adverse hemodynamic effects of anesthesia, head-up tilt, and carbon dioxide pneumoperitoneum during laparoscopic cholecystectomy. *Surg Endosc*. 2000;14(3):272–277.

O'Malley C, Cunningham AJ. Physiologic changes during laparoscopy. *Anesthesiol Clin North America*. 2001;19(1):1–19.

Ost MC, Tan BJ, Lee BR. Urologic laparoscopy: basic physiologic considerations and immunological consequences. *J Urol.* 2005;174(4):1183–1188.

Sosa RE, Weingram J. Physiologic considerations in laparoscopic surgery. *J Endourol.* 1992;6:285–287.

C. Intraoperative Management

C.1. What is the anesthetic technique of choice for laparoscopy? Why?

The technique of choice for laparoscopy is general anesthesia with a cuffed endotracheal tube and controlled positive pressure ventilation, because of the following reasons:

- Duration may be long.
- Patient may be anxious.
- The Trendelenburg position may cause respiratory compromise and dyspnea in the awake or in the spontaneously breathing patient with abdominal contents under pressure. The obese patient may be especially uncomfortable in this position.
- A nasogastric or orogastric tube difficult to insert in a conscious patient is necessary to decompress the stomach and minimize the risk of aspiration or perforation by trocars. CO_2, as with N_2O, diffuses into the stomach.
- However, perhaps the most important reason relates to muscle relaxation. Muscle relaxation and paralysis are necessary because the increase in intra-abdominal pressure and splinting of the diaphragm make spontaneous breathing difficult. It provides a quieter surgical field and better surgical exposure. "Bucking" increases negative pressure in the chest, which increases the risk of pneumothorax or gas dissection. Coughing can further increase pressure in the abdomen and cause movement of, and perforation by, intra-abdominal instruments. Moreover, muscle relaxation is necessary to control and augment ventilation to compensate for the hypercarbia and respiratory acidosis that results from absorption of CO_2.

Brull SJ. Anesthetic considerations for laparoscopic procedures. *ASA Refresher Courses in Anesthesiology.* Vol. 23. Park Ridge, IL: American Society of Anesthesiologists; 1995:15–28.

Chassard D, Berrada K, Tournadre J-P, et al. The effects of neuromuscular block on peak airway pressure and abdominal elastance during pneumoperitoneum. *Anesth Analg.* 1996;82:525–527.

Chui PT, Gin T, Oh TE. Anaesthesia for laparoscopic general surgery. *Anaesth Intensive Care.* 1993;21:163–171.

Whalley DG, Berrigan MJ. Anesthesia for radical prostatectomy, cystectomy, nephrectomy, pheochromocytoma, and laparoscopic procedures. *Anesthesiol Clin North America.* 2000;18(4):899–917.

C.2. Can a laryngeal mask airway (LMA) be used?

Although successful use of the LMA has been reported by several British groups for very brief laparoscopic procedures in healthy patients, its use is not recommended. The LMA does not protect against aspiration. It also limits the ability to apply positive pressure ventilation and interferes with the use of an orogastric tube.

Bapat PP, Verghese C. Laryngeal mask airway and the incidence of regurgitation during gynecological laparoscopies. *Anesth Analg.* 1997;85:139–143.

Brimacombe J, Keller C, Berry A. Gastric insufflation with the ProSeal laryngeal mask. *Anesth Analg.* 2001;92(6):1614–1615.

C.3. What anesthetic agents or adjuvant drugs are recommended for laparoscopy? Are any anesthetic agents contraindicated?

Almost any combination that provides amnesia, analgesia, and paralysis is suitable. Because closure of a laparoscopic procedure may be abrupt, because patients may be discharged soon after surgery, and because a large painful (stimulating) incision is absent, the most common combination probably includes an inhalation agent, a medium-duration narcotic, and an intermediate-acting muscle relaxant.

Use of an antiemetic is recommended to counteract the nausea resulting from peritoneal stimulation and bowel distention (secondary to diffusion of CO_2 into the bowel). Small doses of the antiemetic droperidol had been used effectively because it potentiated sedation, was long acting, could be given early in the procedure, and, as an α-blocker, helped counteract the hypertensive effects of systemic CO_2. Newer antiemetics include such 5-HT_3 receptor antagonists as ondansetron and dolasetron. These may be combined with dexamethasone.

Propofol also has an HT_3 antiemetic effect. However, a propofol-based maintenance anesthetic, when combined with neuromuscular block, may not adequately prevent patient awareness. A bispectral index (BIS) monitor may be helpful in that situation.

A vagolytic drug should be at hand because acute stretching of the peritoneum may cause reflex bradycardia. This is more likely to occur in young women than in older adults.

Halothane is the only anesthetic that should probably be avoided because it may cause arrhythmias in the presence of hypercarbia. Hypnotics and sedatives should be used cautiously in older adults because their duration may be prolonged.

Scuderi PE, D'Angelo R, Harris L, et al. Small-dose propofol by continuous infusion does not prevent postoperative vomiting in females undergoing outpatient laparoscopy. *Anesth Analg.* 1997;84:71–75.

Seed RF, Shakespeare TF, Muldoon MJ. Carbon dioxide homeostasis during anaesthesia for laparoscopy. *Anaesthesia.* 1970;25:223–231.

C.4. Should nitrous oxide (N_2O) be used during laparoscopy? What are the pros and cons? Does N_2O cause bowel distention during laparoscopy? Does N_2O cause nausea and vomiting after laparoscopy?

The use of N_2O has been considered controversial. The controversies surrounding laparoscopic use of N_2O center on the causes of bowel distention during surgery and nausea and vomiting postoperatively.

In examining the issue of bowel distention with N_2O, note the following. The diffusion capacity of N_2O is approximately 14 times that of O_2 and 28 times that of nitrogen (see Table 26.1). Therefore, in a closed space that contains air, N_2O enters faster than N_2 can leave, thereby increasing the size of the closed space. It has been shown that the volume of an enclosed intestinal air pocket can be doubled by inhalation of 70% N_2O in 2 hours and up to tripled in 4 hours. When N_2O is limited to 50%, pocket volume increases no more than 50%. A much more rapid increase in gas volume occurs in the pleural space, where volume was shown to double in 10 minutes, triple in 45 minutes, and quadruple in 2 hours. The faster rate of pleural gas expansion as compared to bowel gas expansion may in part be due to the greater blood flow to the pleura, and possibly due to direct diffusion of N_2O from the alveoli adjacent to the pleura.

However, during laparoscopy, we are concerned about CO_2 pockets not air pockets. N_2O, which has a diffusion capacity almost as great as CO_2, will diffuse from the bloodstream into the intraperitoneal pocket of 100% CO_2 at a rate determined

by its solubility in water, its diffusing capacity through an aqueous membrane, and its pressure gradients (as discussed in section A.13). Similarly, CO_2 will leave the peritoneal cavity according to its pressure gradients and solubility and diffusion characteristics. Eventually, the amount of N_2O found in the peritoneal cavity can be significant, and theoretically it can form an ignition hazard. (However, Hunter states that it is necessary for methane or hydrogen to occupy at least 5.5% of the gas volume for nitrous oxide to support combustion, a condition that does not naturally occur.)

In the situation of an air pocket in the bowel, it is well known that N_2O will diffuse in according to its gradients, thereby enlarging the pocket. However, few realize that even in the absence of N_2O, CO_2 also will diffuse into this pocket and expand it in a manner that is clinically indistinguishable from N_2O.

N_2O is often blamed for a distended bowel during laparoscopy, without realizing that CO_2 is equally capable of diffusing into and distending the bowel. In a double-blinded study of bowel distention in patients undergoing laparoscopic cholecystectomy with either isoflurane 70%-N_2O-O_2 or isoflurane-air-O_2, the surgeon was able to identify the use of N_2O correctly only 44% of the time. In addition, postoperative nausea and vomiting was independent of the use of N_2O, because the incidence was similar in both groups. Another study found no difference in the incidence of postoperative nausea and vomiting between groups receiving propofol-air-O_2 or propofol-N_2O-O_2 in gynecologic laparoscopy. In fact, the propofol-N_2O-O_2 group had the advantages of significantly more rapid emergence, use of 30% less propofol, additional analgesia, and less risk of awareness.

Because of these issues, it is recommended that nitrous oxide, if used, be limited to not more than 50% of the inspired mixture during laparoscopy. Alternatively, a mixture of 75% air and 25% oxygen (FIO_2 = 40%) is probably a wiser choice.

Arellano RJ, Pole ML, Rafuse SE, et al. Omission of nitrous oxide from a propofol-based anesthetic does not affect the recovery of women undergoing outpatient gynecological surgery. *Anesthesiology*. 2000;93(2):332–339.

Diemunsch PA, Torp KD, Van Dorsselaer T, et al. Nitrous oxide fraction in the carbon dioxide pneumoperitoneum during laparoscopy under general inhaled anesthesia in pigs. *Anesth Analg*. 2000;90:951–953.

Diemunsch PA, Van Dorsselaer T, Torp KD, et al. Calibrated pneumoperitoneal venting to prevent N_2O accumulation in the CO_2 pneumoperitoneum during laparoscopy with inhaled anesthesia: an experimental studying pigs. *Anesth Analg*. 2002;94:1014–1018.

Eger EI II, Saidman LJ. Hazards of nitrous oxide anesthesia in bowel obstruction and pneumothorax. *Anesthesiology*. 1965;26:61–66.

Hunter JG, Staheli J, Oddsdottir M, et al. Nitrous oxide pneumoperitoneum revisited. Is there a risk of combustion? *Surg Endosc*. 1995;9:501–504.

Munson ES. Transfer of nitrous oxide into body air cavities. *Br J Anaesth*. 1974;46:202–209.

Neuman GG, Sidebotham G, Negoianu E, et al. Laparoscopic explosion hazards with N_2O. *Anesthesiology*. 1993;78:875–879.

Sukhani R, Lurie J, Jabamoni R. Propofol for ambulatory gynecologic laparoscopy: does omission of nitrous oxide alter postoperative emetic sequelae and recovery? *Anesth Analg*. 1994;78:831–835.

Taylor E, Feinstein R, White PF, et al. Anesthesia for laparoscopic cholecystectomy. Is nitrous oxide contraindicated? *Anesthesiology*. 1992;76:541–543.

C.5. Can laparoscopy be performed under local anesthesia or regional anesthesia?

Yes. However, under local anesthesia, CO_2 may cause pain intraperitoneally, which is referred to the shoulder. It is for this reason that N_2O, which is nonirritating to the

peritoneum, had been used as the insufflating gas for very brief diagnostic laparoscopy under local anesthesia without cautery. However, rapid peritoneal distention causes nausea, which may be worsened without a nasogastric tube. Because of patient discomfort, the surgeon may obtain suboptimal visualization of the surgical field. Also the possibility, although remote, of having to open the abdomen speaks against local anesthesia.

Regional anesthesia can be used for laparoscopy. However, it too has serious drawbacks. It requires a high level of sensory block, possibly causing dyspnea in the Trendelenburg position. A nasogastric tube may not be tolerated. Hyperventilation in response to hypercarbia may cause too much movement in the surgical field, and spontaneous ventilation may be inadequate to compensate for hypercarbia in the Trendelenburg position. Because the systemic response to hypercarbia is mediated primarily through sympathetic stimulation, the sympathetic denervation resulting from high regional anesthesia will result in hypotension and decreased cardiac output rather than the hypertension and increased cardiac output usually seen with general anesthesia.

Use of IV analgesics or propofol during regional anesthesia may result in respiratory depression or obstruction, especially in steep Trendelenburg position. Hypoxia in the presence of hypercarbia may have serious cardiovascular consequences.

Collins LM, Vaghadia H. Regional anesthesia for laparoscopy. *Anesthesiol Clin North America*. 2001;19(1):43–55.

Fishburne JI. Anesthesia for laparoscopy: considerations, complications and techniques. *J Reprod Med*. 1978;21:37–40.

Vaghadia H, Solylo MA, Henderson CL, et al. Selective spinal anesthesia for outpatient laparoscopy. II: epinephrine and spinal cord function. *Can J Anaesth*. 2001;48: 261–266.

C.6. What monitors and devices would you apply to the patient? Why?

The usual intraoperative monitors, including standard 5-lead ECG with ST trending, systemic blood pressure (BP) using automated oscillometry, pulse oximetry, capnography, a nerve stimulator, and indicators of inspired oxygen fraction, minute ventilation, and peak airway pressures are necessary. An esophageal probe may be used for both temperature monitoring (optimal at the distal esophagus) and for breath, heart, and murmur sound monitoring (at heart level). Body temperature should be maintained with a forced warm air heating blanket, warmed intravenous fluids, or other means. (For robotic procedures, we place the warming blanket under the patient.) Rarely, central venous pressure (CVP), pulmonary artery pressure, pulmonary artery occlusion pressure (PAOP) and cardiac output may be measured in patients with severe cardiac or pulmonary abnormalities. A BIS monitor may be used. Other possibilities include Doppler, transesophageal echocardiography, and noninvasive assessment of cardiac output by thoracic bioimpedance or thoracic ultrasound. An arterial line is suggested during longer, more complex laparoscopic procedures in sicker (ASA classes III and IV) patients.

Intermittent sequential compression antiembolic stockings should be applied. Shoulder braces or adhesive taping are used for support in the Trendelenburg position. After the patient is asleep, a nasogastric or orogastric tube and a Foley catheter is inserted for decompression of stomach and bladder. Use of an orogastric tube is not optional. In addition to the danger of regurgitation from the increased abdominal pressure, reports have been made of stomach perforation by trocars. The orogastric tube should not be clamped after initial placement, and intermittent suctioning should continue, because CO_2 gas continues to diffuse into the stomach and distend it.

In addition to mechanical monitoring, visual and tactile monitoring are necessary during laparoscopy. Skin color, skin turgor, and capillary refill should be monitored because they can change abruptly. The head, neck, and upper chest may assume a purplish color in the dependent position, especially during hypercarbia. The upper chest wall should be checked periodically for subcutaneous emphysema. The cornea and conjunctiva should be checked periodically for edema, especially in the Trendelenburg position, and also whenever oliguria occurs because the extent of the edema may influence your decision on when to extubate.

It is important to maintain accurate data on the volume of fluids infused, and the patient's hourly or half-hourly urine output, along with observations on its color and concentration. Despite adequate hydration, oliguria frequently occurs during pneumoperitoneum, especially at intra-abdominal pressures approaching or exceeding 15 mm Hg. The acute increase in intra-abdominal pressure is transmitted to the kidneys, and is believed to cause shunting from the cortex to the medulla of the kidney, resulting in decreased urine output. Diuresis usually occurs rapidly on release of intra-abdominal pressure.

Jacobs VR, Morrison JE, Mettler L, et al. Measurement of CO_2 hypothermia during laparoscopy and pelviscopy: how cold it gets and how to prevent it? *J Am Assoc Gynecol Laparosc.* 1999;6:289–295.

Ogunnaike BO, Jones SB, Jones DB, et al. Anesthetic considerations for bariatric surgery. *Anesth Analg.* 2002;95(6):1793–1805.

Tournadre JP, Chassard D, Berrada KR, et al. Effect of pneumoperitoneum and Trendelenburg position on lower oesophageal sphincter pressure. *Br J Anaesth.* 1996; 76:130–132.

Weingram J. Laparoscopic and laser surgery. In: Malhotra V, ed. *Anesthesia for Renal and Genito-urologic Surgery.* New York: McGraw-Hill; 1996:166–168.

C.7. How is the patient to be positioned? What special precautions are required for robotic laparoscopy?

In pyeloplasties the side to be worked on usually is elevated, enabling gravity to assist in separating the organs and allowing blood to pool away from the operative field. For other laparoscopies, the patient may be supine, in the Trendelenburg position (with possible lateral rotation) for urology; in dorsolithotomy for gynecology; in the head-up position for upper gastrointestinal and biliary tract surgery; and in the lateral decubitus position for thoracoscopy, nephrectomy, and adrenalectomy. For standard laparoscopy, you may or may not be able to keep one or both arms out on boards, depending upon the procedure and the surgeon's needs.

In robotically assisted laparoscopy, it is especially important to check that all lines (IVs, A-line if present) as well as BP cuff, ECG leads, and pulse oximeter are functioning properly after the arms have been carefully padded and tucked at the patient's sides. This must be done before the patient is lowered into Trendelenburg position. Once the robot is locked into position, you will no longer have access to check the arms or look under the drapes. It is a good idea to cut off the clamps on the IV tubing that may press into the patient's skin while the arms are tightly tucked.

Next, after satisfactory general endotracheal anesthesia has been obtained, the surgeons may place towels or sponges across the patient's chest, followed by criss-crossing of wide adhesive tape reaching from one side of the table and patient's chest to the opposite shoulder and opposite side of the table. This X-formation is designed to secure the patient to the table. While the surgeons are applying the tape, it is recommended that you put your hand under the chest sponge to make sure that the tape is not tight enough to restrict chest expansion. (Padded shoulder braces may

be used instead of the tapes, but the incidence of brachial plexus injury is higher with these.)

With the knees flexed in padded leg holders, the patient is now carefully lowered into steep Trendelenburg position.

Kalmar AF, Foubert L, Hendrickx JF, et al. Influence of steep Trendelenburg position and CO_2 pneumoperitoneum on cardiovascular, cerebrovascular, and respiratory homeostasis during robotic prostatectomy. *Br J Anaesth.* 2010;104(4):433–439.

Klauschie J, Wechter ME, Jacob K, et al. Use of anti-skid material and patient positioning to prevent patient shifting during robotic-assisted gynecologic procedures. *J Minim Invasive Gynecol.* 2010;17(4):504–507.

Phong SV, Koh LK. Anaesthesia for robotic-assisted radical prostatectomy: considerations for laparoscopy in the Trendelenburg position. *Anaesth Intensive Care.* 2007;35(2):281–285.

C.8. How will you ventilate the patient? What are the respiratory and circulatory effects of the Trendelenburg position during laparoscopy?

Respiratory

Vital capacity and FRC are reduced. The abdominal contents restrict movement of the diaphragm, especially in the obese and in older adults. Decreased compliance, increased ventilation–perfusion abnormalities, and cephalad displacement of the mediastinum commonly occur.

Circulatory

In healthy patients, Trendelenburg position results in minimal circulatory changes. Venous return and cardiac output are increased, whereas CVP, pulmonary artery occlusion pressure (PAOP), systemic vascular resistance (SVR), and heart rate are essentially unchanged. In patients with cardiovascular disease, the Trendelenburg position may result in increased CVP, PAOP, and decreased cardiac output. The increase in venous return and myocardial oxygen demand that occurs in severe cardiovascular disease can precipitate acute heart failure.

These respiratory and circulatory changes caused by the Trendelenberg position are further amplified by the CO_2 insufflation. Ventilation may become difficult, especially in obese patients. Use of positive end-expiratory pressure (PEEP) is advised. To prevent peak inspiratory pressures from becoming excessive, switching from volume-controlled to pressure-controlled ventilation may be warranted.

Battillo JA, Hendler MA. Effects of positioning during anesthesia. *Int Anesthesiol Clin.* 1993;31:67–86.

Cadi P, Guenoun T, Joumois D, et al. Pressure-controlled ventilation improves oxygenation during laparoscopic obesity surgery compared with volume-controlled ventilation. *Br J Anaesth.* 2008;100(5):709–716.

Freeza EE. The lithotomy versus the supine position for laparoscopic advanced surgeries: a historical review. *J Laparoendosc Adv Surg Tech A.* 2005;15(2):140–144.

Kim JY, Shin CS, Kim HS, et al. Positive end-expiratory pressure in pressure-controlled ventilation improves ventilatory and oxygenation parameters during laparoscopic cholecystectomy. *Surg Endosc.* 2010;24(5):1099–1103.

Maartin JT, Warner MA, eds. *Positioning in Anesthesia and Surgery.* 3rd ed. Philadelphia: WB Saunders;1997:95–123.

Ogurlu M, Kucuk M, Bilgin F, et al. Pressure-controlled vs volume-controlled ventilation during laparoscopic gynecologic surgery. *J Minim Invasive Gynecol.* 2010;17(3):295–300.

C.9. What two techniques are available for initial laparoscopic access to the peritoneal cavity? What anesthetic problems can arise during insufflation?

Pneumoperitoneum can be achieved by a "blind" or closed technique of percutaneous insertion of the 2-mm diameter hollow Veress needle, which after verification of correct positioning, is connected to the CO_2 insufflator. (After Veress needle insertion, the first trocar is also inserted blindly.)

Alternatively, if previous surgery or adhesions are to be avoided, an "open" approach is taken. A mini incision is created, and the blunt-tipped Hasson cannula is inserted without prior pneumoperitoneum. The laparoscope is then inserted through the trocar to verify the intra-abdominal position before insufflation begins.

During insufflation, abdominal distention should be evenly distributed in all four quadrants. Respiratory variations of intraperitoneal pressure should be visible, and peak inspiratory pressures will gradually increase as the abdomen distends. It is at this time that the anesthesiologist should be alert to the possibility of vagally mediated reflexes. Bronchospasm, bradycardia, and even sinus arrest have been reported, especially in young women. Visceral and vascular perforations are also well-reported complications, especially with the blind technique. Cardiovascular collapse and gas emboli have been reported when CO_2 has been inadvertently insufflated directly into a blood vessel.

Merlin TL, Hiller JE, Maddern GJ, et al. Systematic review of the safety and effectiveness of methods used to establish pneumoperitoneum in laparoscopic surgery. *Br J Surg.* 2003;90(6):688–679.

Schwartz ML, Drew RL, Andersen JN. Induction of pneumoperitoneum in morbidly obese patients. *Obes Surg.* 2003;13(4):601–604.

Teoh B, Sen R, Abbott J. An evaluation of four tests used to ascertain Veress needle placement at closed laparoscopy. *J Minim Invasive Gynecol.* 2005;12(2):153–158.

Vilos GA, Vilos AG. Safe laparoscopic entry guided by Veress needle CO_2 insufflation pressure. *J Am Assoc Gynecol Laparosc.* 2003;10(3):415–420.

C.10. What intravenous (IV) solution and how much fluid volume do you plan to deliver?

Large-bore intravenous catheters should be placed because of the possibility of major hemorrhage. The amount of IV fluid infused is of vital importance, especially in older adults. Transient oliguria during laparoscopy is common. In our early cases, we increased our infusion rate in response to waning urine output, and we hydrated intraperitoneal laparoscopic cases as if they were open intraperitoneal cases. After several cases of "unexplained" pulmonary edema in the PACU we concluded that the oliguria seen in laparoscopy is not related to volume depletion, and we have decreased our fluid replacement to approximately 4 mL/kg/hour of Ringer's lactate solution, depending on the patient's preoperative hemodynamic status and the volume of residual intraperitoneal irrigation fluid used by the surgeon. In calculating fluid requirements during laparoscopy, it is important to remember that much less "third-spacing" occurs than in open surgery, no fluid loss is caused by evaporation, and the volume of retained (after suctioning) intraperitoneal saline used for irrigation by the surgeon should be added to the final total volume of infused IV fluids. In addition, the intra-abdominal humidification of the insufflated dry CO_2 gas results in only a negligible insensible water loss.

After pneumoperitoneum is ended, diuresis occurs promptly and renal function quickly returns to normal (see section C.22).

For robotic laparoscopies, surgeons prefer that IV fluids are minimized until the anastomoses are completed. This keeps excessive fluids out of the surgical field and also helps prevent edema of the face, eyes, and larynx while in steep Trendelenberg

position. After the anastomoses are complete, the surgeons prefer that we then hydrate the patient. At our institution, the average duration for robotic prostatectomy is 3 to 3½ hours, the average blood loss is under 200 mL, and the usual fluid replacement is 3 to 3.5 L of lactated Ringer's solution.

Concha MR, Mertz VF, Cortinez LI, et al. The volume of lactated Ringer's solution required to maintain preload and cardiac index during open and laparoscopic surgery. *Anesth Analg.* 2009;108(2):616–622.

Gomez Dammeier BH, Karanik E, et al. Anuria during pneumoperitoneum in infants and children: a prospective study. *J Pediatr Surg.* 2005;40(9):1454–1458.

London ET, Ho HS, Neuhaus AM, et al. Effect of intravascular volume expansion on renal function during prolonged CO_2 pneumoperitoneum. *Ann Surg.* 2000;231:195–201.

Muzii L, Bellati F, Manci N, et al. Ringer's lactate solution remains in the peritoneal cavity after laparoscopy longer than expected. *Fertil Steril.* 2005;84(1):148–153.

Olsson J, Svensen CH, Hahn RG. The volume kinetics of acetated Ringer's solution during laparoscopic cholecystectomy. *Anesth Analg.* 2004;99(6):1854–1860.

Sjostrand F, Hahn RG. Volume kinetics of glucose 2.5% solution during laparoscopic cholecystectomy. *Br J Anaesth.* 2004;92(4):485–492.

Tittel A, Schippers E, Grablowitz V, et al. Intraabdominal humidity and electromyographic activity of the gastrointestinal tract. Laparoscopy versus laparotomy. *Surg Endosc.* 1995;9:786–790.

Weingram J, Sosa RE, Stein B. Oliguria during laparoscopic pelvic lymph node dissection. *Anesth Analg.* 1996;82:S484.

C.11. What is the purpose of the heparinized saline irrigation-suction device used by the surgeon and why should you be concerned with it?

The heparinized saline irrigation-suction device (5 L delivered by pressurized bag) is used by the surgeons to retard clot formation in the abdomen, to remove blood from the field, and to remove smoke from electrocautery. It takes the place of lap pads and sponges in open surgery. If the tip of the suction device is not kept under the fluid level, CO_2 gas will be aspirated and exposure of the field will be lost.

Its further significance to the anesthesiologist is twofold. First, the difference between the volume of saline missing from the irrigation bag and the volume in the suction collection bottle must be considered as part of the patient's fluid intake. Second, the temperature of the saline solution intraperitoneally can alter the patient's body temperature.

Moore SS, Green CR, Wang FL, et al. The role of irrigation in the development of hypothermia during laparoscopic surgery. *Am J Obstet Gynecol.* 1997;176:598–602.

C.12. Under what circumstances should laparoscopy be converted to laparotomy?

Laparotomy should be performed immediately in cases of bleeding or major organ damage. Other circumstances include persistent problems with inadequate exposure, procedure beyond the surgeon's capability, procedure taking too long, inability to create or maintain pneumoperitoneum, patient deterioration, equipment failure, and discovery of other unsuspected disease.

Tabboush ZS. When hypotension during laparoscopic cholecystectomy indicates termination of the laparoscopy [Letter]. *Anesth Analg.* 1994;79:195–196.

C.13. What are the arterial to end-tidal CO_2 gradients ($Paco_2$–$PetCO_2$) in the normal awake patient? What is the cause of the gradient? Does the gradient change during laparoscopy? Why?

In the awake person at rest, the normal arterial to end-tidal Pco_2 difference is small, perhaps ranging from 2 to 6 mm Hg. The gradient and its variations are measures of the alveolar dead space. The gradient is the sum of the difference between the arterial and alveolar CO_2 plus the difference between the alveolar and end-tidal CO_2. It is commonly increased in emphysema. The difference is increased when underperfused alveoli are ventilated, as often occurs during hyperventilation in laparoscopy.

The total physiologic dead space consists of the anatomic dead space (passageways that do not participate in gas exchange, approximately 150 mL) and the alveolar dead space (i.e., underperfused alveoli). The alveolar dead space gas is expired at the same time as the alveolar ideal gas from well-perfused alveoli in equilibrium with pulmonary capillary blood. The dilution of the ideal alveolar gas by the alveolar dead space gas is represented by the end-tidal CO_2.

Some of the factors resulting in a relative increase in ventilation-to-perfusion ratio include mechanical ventilation, hyperventilation, rapid or shallow ventilation, and Trendelenburg or lateral decubitus position.

Some of the factors resulting in a relative decrease in perfusion-to-ventilation ratio include hypotension, decreased cardiac output, myocardial depression from inhalational anesthetics, pulmonary emboli, high positive airway pressure, and ablation of the hypoxic pulmonary vasoconstriction reflex.

Christensen MA, Bloom J, Sutton KR. Comparing arterial and end-tidal carbon dioxide values in hyperventilated neurosurgical patients. *Am J Crit Care*. 1995;4:116–121.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 6th ed. Philadelphia: Butterworth-Heinemann; 2005:157–158, 318–319.

C.14. Is an arterial line necessary? Why? Does end-tidal CO_2 tension accurately reflect arterial CO_2 tension? Under what circumstances may the $PetCO_2$ exceed the $Paco_2$? Why?

An arterial line is recommended whenever the laparoscopic procedure is unusually complex, long or when the patient has significant cardiopulmonary disease. In such cases, ventilation–perfusion abnormalities, intraoperative hypoxemia, marked hypercarbia, or high airway pressures may be expected. During these situations, and possibly in all laparoscopies, an unsteady state exists with respect to CO_2, and the assumption that $PetCO_2$ may accurately reflect a predictable relationship to $Paco_2$ is not valid.

End-tidal CO_2 tension can either estimate $Paco_2$; or, more often, it may underestimate $Paco_2$; or, less often, it may even exceed $Paco_2$. Furthermore, the values for these two measurements do not always change proportionally nor do they always change in the same direction. The relationship between $PetCO_2$ and $Paco_2$ varies during the course of the procedure. At the beginning of insufflation, $PetCO_2$ can be used as a rough estimate of $Paco_2$. However, when redistribution of the excess CO_2 from the well-perfused tissues to the less well-perfused tissues begins, $PetCO_2$ begins to underestimate the $Paco_2$. Characteristically, the arterial to end-tidal CO_2 difference progressively increases as hyperventilation (and dead space) increases.

Especially during strenuous exercise when metabolic CO_2 production is increased and during laparoscopy when excess exogenous CO_2 must be excreted, the $PetCO_2$ may be found to exceed the $Paco_2$. This condition has also been reported in a hyperventilating patient during cesarean section. This occurs because the $Paco_2$ fluctuates during each deep breath and may not represent the highest value at that

instant, whereas the $P_{ET}CO_2$ shows the maximal value (i.e., because of tidal ventilation and pulsatile blood flow in exercise, $P_{ET}CO_2$ may exceed mean alveolar and arterial CO_2).

Bhavani-Shankar K, Steinbrook RA, Brooks DC, et al. Arterial to end-tidal carbon dioxide difference during laparoscopic surgery in pregnancy. *Anesthesiology*. 2000;93(2): 370–373.

Gravenstein JS, ed. *Gas Monitoring and Pulse Oximetry*. Boston: Butterworth-Heinemann; 1990:106–116.

Jones NL, Robertson DG, Kane JW. Difference between end-tidal and arterial P_{CO_2} in exercise. *J Appl Physiol*. 1979;47:954–960.

Lee TS. End-tidal partial pressure of carbon dioxide does not accurately reflect $Paco_2$ in rabbits treated with acetazolamide during anaesthesia. *Br J Anaesth*. 1994;73: 225–226.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 6th ed. Philadelphia: Butterworth-Heinemann; 2005:157–158, 318–319.

Scheid P, Meyer M, Piper J. Arterial-expired P_{CO_2} differences in the dog during acute hypercapnia. *J Appl Physiol*. 1979;47:1074–1078.

Shankar KB, Moseley H, Kumar Y, et al. Arterial to end-tidal carbon dioxide tension difference during caesarean section anaesthesia. *Anaesthesia*. 1986;41:698–702.

Strang CM, Hachenberg T, Freden F, et al. Development of atelectasis and arterial to end-tidal PCO_2 difference in a porcine model of pneumoperitoneum. *Br J Anaesth*. 2009;103(2);298–303.

Wulkan ML, Vasudevan SA. Is end-tidal CO_2 an accurate measure of arterial CO_2 during laparoscopic procedures in children and neonates with cyanotic congenital heart disease? *J Pediatr Surg*. 2001;36(8):1234–1236.

C.15. What are the possible causes of hypercarbia?

- Hypoventilation.
- CO_2 in the inspired gas—rebreathing endogenous CO_2 will increase $Paco_2$ by 3 to 6 mm Hg per minute.
- Increased endogenous CO_2 production or from exogenous CO_2 supply—occurring in the hypermetabolic states of malignant hyperpyrexia, fever, and hyperthyroidism; and in laparoscopy, or following administration of bicarbonate or lactate (1 ampule of 50 mEq of bicarbonate liberates more than 1 L of CO_2).
- Increased dead space (rare) as in pulmonary embolism, ventilation of a lung cyst, or in advanced COPD.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 6th ed. Philadelphia: Butterworth-Heinemann; 2005:140, 328.

Wolf JS Jr, Clayman RV, Monk TG, et al. Carbon dioxide absorption during laparoscopic pelvic operation. *J Am Coll Surg*. 1995;180:555–560.

C.16. What factors play a role in the unusually rapid and marked elevation of CO_2 that is sometimes seen in laparoscopy?

- Patients with significant cardiopulmonary disease
- Intra-abdominal pressure greater than 15 mm Hg
- Presence of subcutaneous emphysema
- Retroperitoneal rather than intraperitoneal approach
- Long duration of laparoscopy

Bozkurt P, Kaya G, Yeker Y, et al. Arterial carbon dioxide markedly increases during diagnostic laparoscopy in portal hypertensive children. *Anesth Analg.* 2002;95(5):1236–1240.

Liem KS, Kallewaard JW, deSmet AM, et al. Does hypercarbia develop faster during laparoscopic herniorrhaphy than during laparoscopic cholecystectomy? Assessment with continuous blood gas monitoring. *Anesth Analg.* 1995;81:1243–1249.

C.17. How rapidly does the $Paco_2$ rise in the apneic patient (endogenous CO_2)? How rapidly does the $Paco_2$ rise if 5% CO_2 gas is inhaled (exogenous)? How rapidly can the CO_2 rise during laparoscopy? What factors explain the differences?

In the apneic patient, $Paco_2$ rises at the rate of 3 to 6 mm Hg per minute. Rebreathing, or inhalation of 5% CO_2 in oxygen, causes a much more rapid rise in $Paco_2$ up to 8 to 10 mm Hg per minute. The difference in rate of rise between endogenous and exogenous CO_2 is explained by the presence of large body stores of CO_2. Approximately 120 L of CO_2 exist in the body (100 times the amount for oxygen) distributed among well-perfused tissue (e.g., blood, brain), moderately perfused tissue (e.g., muscle), and poorly perfused tissue (e.g., fat, bone). These storage places adjust slowly to acute CO_2 changes. In the steady state, the amount of CO_2 produced metabolically in the body is equal to the amount expired through the lungs, and there is no change in the body stores of CO_2. During laparoscopy an unsteady state exists, with the rate of rise of Pco_2 being greatest during the first 20 to 30 minutes. After that time, new equilibrium levels are reached between the different compartments, and the Pco_2 rate of rise is slower.

Frumin et al. studied the hypercarbic state during their classic study of apneic oxygenation. In paralyzed apneic intubated denitrogenated oxygenated patients receiving only thiopental for amnesia, Frumin et al. demonstrated at least a 3-mm Hg average rise in $Paco_2$ per minute and an ultimate $Paco_2$ as high as 250 mm Hg (pH 6.72) while maintaining 98% to 100% O_2 saturation after 53 minutes of apnea. They also found that the hypercarbia was accompanied by hypertension (mean arterial pressure rise of 26%, followed by a fall of 14% on return of respirations and normocarbia). Other features accompanying apneic hypercarbic hypertension included normal sinus rhythm with an essentially unchanged rate, rising arterial epinephrine and norepinephrine concentrations, and rising arterial potassium levels (which rose still further after ventilation and normocarbia resumed) with unchanged sodium levels.

Frumin J, Epstein RM, Cohen G. Apneic oxygenation in man. *Anesthesiology.* 1959;20:789–798.

Lumb AB. *Nunn's Applied Respiratory Physiology.* 6th ed. Philadelphia: Butterworth-Heinemann; 2005:160, 318–319.

C.18. What are the direct and indirect effects of hypercarbia on the cardiovascular system? How are these effects altered by increased intra-abdominal pressure and patient position?

The effects of hypercarbia on the circulatory system are complex and often contradictory. At the cellular level, hypercarbia is a direct depressor of myocardial contractility and rate of contraction, and it is also a direct stimulant of myocardial irritability and arrhythmicity. These effects may be enhanced by the reduced pH caused by hypercarbia.

The direct effect of hypercarbia on isolated or denervated blood vessels is a diminished responsiveness to catecholamines and vasodilation especially on the venous side, leading to peripheral pooling, decreased venous return, and decreased cardiac output. The exception to the dilatory effect of hypercarbia and acidosis on blood vessels exists in the pulmonary vessels, which undergo vasoconstriction. It appears,

however, that the effects on the pulmonary vessels are actually due to acidosis rather than hypercarbia because if the pH is kept constant while the P_{CO_2} rises, then pulmonary vascular resistance (PVR) does not change.

In the patient, however, the direct or local effects of CO_2 can be overshadowed by a variety of systemic effects. Simultaneous with these local or direct effects, hypercarbia causes profound systemic changes secondary to stimulation of the central nervous system and sympathoadrenal system. The net effect usually includes an increase in cardiac output, heart rate, force of myocardial contraction, BP, CVP, vasoconstriction in the pulmonary (capacitance) vessels, and decreased peripheral resistance. The rise in cardiac output of up to 50% exceeds the rise in BP, because of the drop in peripheral resistance and increase in blood flow primarily in the cerebral and coronary circulations. This net stimulatory effect accompanies the elevation of P_{aCO_2} up to approximately 90 mm Hg. Above this level, further increases in CO_2 cause a marked drop in response.

In a normal anesthetized human breathing 7% to 15% inspired CO_2, these stimulatory changes were shown to correspond primarily to rising plasma concentrations of epinephrine and norepinephrine. When the sympathoadrenal response was prevented by subarachnoid block, ganglioplegics, or α-adrenergic blockers, the cardiovascular response to inhaled CO_2 was hypotension and decreased cardiac output. The stimulatory response also is diminished by general anesthesia.

Hypercarbia can cause arrhythmias during epinephrine infiltrations or in the presence of halothane but not other anesthetics. Other than in these two circumstances, hypercarbia is not arrhythmogenic unless hypoxia also is present.

The full range of possible effects of hypercarbia on the cardiovascular system are subject to many influences. Healthy (ASA class I) patients are less likely than ASA class III patients to undergo extreme changes. Similarly, a brief surgical duration, head-up positioning, low intra-abdominal pressures, and intraperitoneal (rather than extraperitoneal) surgery can limit the range of physiologic and metabolic responses to near normal.

In the patient with marginal cardiovascular function, however, peritoneal insufflation can result in significant increase in cardiac workload. In this situation, transesophageal echocardiography may provide a useful noninvasive method of estimation of left ventricular function.

Arrhythmias such as bradycardia, nodal rhythm, or even asystole can follow rapid peritoneal distention and vagal stimulation. In general, BP, pulse, cardiac output, and CVP will increase up to an intra-abdominal pressure of 15 mm Hg. At insufflation pressures of 20 to 30 mm Hg, a decrease in BP, cardiac output, and CVP will occur because of pressure on the inferior vena cava and decreased venous return. Pneumoperitoneum also may induce changes in the cardiac electrical axis, which may affect interpretation of the ECG seen on the monitor during the operation.

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C.19. What are the direct and indirect effects of hypercarbia on the respiratory system? How does the Trendelenburg position and the increased intra-abdominal pressure of pneumoperitoneum alter these effects?

Hypercarbia and acidosis stimulate the respiratory center both directly and indirectly through chemoreceptors, hormones, and autonomic nerves. In the conscious patient breathing oxygen, the maximal stimulating effect occurs at 100 to 150 mm Hg, producing minute volumes of up to 75 L. Above these levels, CO_2 becomes a respiratory depressant. Current anesthetics blunt the stimulatory respiratory response to CO_2. (Diethyl ether, however, the only volatile anesthetic known to stimulate respiration, is reported to have caused a patient to continue to breathe spontaneously at an inadvertent P_{CO_2} of 234 mm Hg.)

In the awake patient, each mm Hg increase in Pa_{CO_2} increases ventilation by 2 to 3 L per minute (if Pa_{O_2} is constant). This response is diminished by anesthesia. Hypercarbia also produces bronchodilatation; acidosis rather than hypercarbia per se, causes pulmonary vascular constriction.

General anesthesia with intubation and mechanical ventilation results in a decrease in FRC, which is caused by loss of muscle tone, diaphragmatic displacement, and loss of thoracic volume. Lung compliance drops, airway pressures increase, and $\dot{V}/\dot{Q}$ abnormalities occur. However, most patients have no difficulty tolerating these changes. These changes are exaggerated in the Trendelenburg position, especially in older adults, the obese, and those with pre-existing cardiopulmonary disease. Intrathoracic, peak inspiratory, and plateau pressures increase and then increase even further when pneumoperitoneum creates an increase in pressure and volume. Endobronchial intubation can occur as a result of cephalad movement of the carina, and it should be ruled out if hypoxemia occurs.

Andersson LE, Baath M, Thorne A, et al. Effect of carbon dioxide pneumoperitoneum on development of atelectasis during anesthesia, examined by spiral computed tomography. *Anesthesiology.* 2005;102(2):293–299.

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Sprung J, Whalley DG, Falcone T, et al. The effects of tidal volume and respiratory rate on oxygenation and respiratory mechanics during laparoscopy in morbidly obese patients. *Anesth Analg.* 2003;97:268–274.

Whalen FX, Gajic O, Thompson GB, et al. The effects of the alveolar recruitment maneuver and positive end-expiratory pressure on arterial oxygenation during laparoscopic bariatric surgery. *Anesth Analg.* 2006;102:298–305.

C.20. What are the direct and indirect effects of hypercarbia on the central nervous system?

The brain is particularly sensitive to changes in $Paco_2$. Slight elevations of CO_2 cause direct cortical depression and increase the threshold for seizures. Higher levels of CO_2 (25% to 30%) stimulate subcortical hypothalamic centers, resulting in increased cortical excitability and seizures. This hyperexcitability level is enhanced by adrenal cortical and medullary hormones released secondary to hypercarbia-induced stimulation of the hypothalamus. Further elevations of CO_2 cause an anesthetic-like state of cortical and subcortical depression.

CO_2 was first used as an anesthetic by Hickman in 1824 and reintroduced by Leake and Waters in 1928. CO_2 caused an N_2O-like narcosis at approximately 90 to 120 mm Hg. However, hypercarbia also causes increased excitability of neurons so that seizures occurred shortly afterward. In dogs, however, general anesthesia is achieved at the higher level of $Paco_2$, approximately 245 mm Hg, probably by intracellular derangements caused by low pH.

CO_2, not H^+, crosses the blood–brain barrier and the brain cell membrane and affects the cell metabolism. Therefore, a change in $Paco_2$ also causes a rapid change in cerebrospinal fluid (CSF) pH. CO_2 is the most important factor in regulating cerebral blood flow (CBF). The relation between CBF and $Paco_2$ is essentially linear from 20 to 100 mm Hg, with maximal vasodilatation at approximately 120 mm Hg. Normal CBF is approximately 12% to 15% of cardiac output, or 50 mL/100 g/minute. For each 1 mm Hg increase in $Paco_2$ between 20 and 80 mm Hg, CBF increases by 2% to 4%. Hypercarbia decreases cerebral vascular resistance, causing CBF to increase.

Hypercarbia causes an increase in intracranial pressure, probably secondary to vasodilation. When the patient is placed in the Trendelenburg position, venous congestion of the head and neck occurs. Additional increases in intra-abdominal and intrathoracic pressures contribute to further increases in intracranial and CSF pressures.

Therefore, an acute rise in intra-abdominal pressure (pneumoperitoneum) causes an immediate rise in intracranial pressure. This occurs through intermediary steps that include compression of the inferior vena cava (resulting in decreased drainage in the lumbar plexus), increased CVP, increased mean arterial pressure, increased intrathoracic pressure, increased venous stasis and increased pressure in the sagittal sinus, and decreased resorption of CSF. Hypercarbia contributes to the increased intracranial pressure, but hyperventilation will not decrease the elevated intracranial pressure until the elevated intra-abdominal pressure is released.

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C.21. What are the neuroendocrine changes that occur during laparoscopy?

Excessive intra-abdominal pressure and hypercarbia may activate the sympathoadrenal axis, resulting in increased plasma levels of epinephrine and norepinephrine. Renin, cortisol, aldosterone, antidiuretic hormone, and atrial natriuretic peptide levels are also increased. In awake patients in the Trendelenburg position, increased secretion of atrial natriuretic peptide occurs, probably in response to increased venous return and atrial stretch. During pneumoperitoneum, however, secretion of atrial natriuretic factor diminishes, suggesting interference with venous return.

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Sood J, Jayaraman L, Kumra VP, et al. Laparoscopic approach to pheochromocytoma: is a lower intraabdominal pressure helpful? *Anesth Analg.* 2006;102:637–641.

C.22. What are the direct and indirect effects of laparoscopy on the renal system?

Oliguria has been observed frequently during laparoscopy despite adequate hydration. Although prerenal causes such as hypovolemia, positive pressure ventilation, and PEEP contribute to oliguria, it is believed that neurohumoral changes (e.g., antidiuretic hormone secretion) secondary to hypercarbia and increased intra-abdominal pressure secondary to insufflation may be responsible. Sympathetic stimulation causes a release of catecholamines, resulting in decreased renal cortical blood flow with shunting of blood to the adrenal medulla, constriction of glomerular afferent arterioles, and decreased glomerular filtration rate. It has been shown recently that when intraperito-

neal insufflation reaches a pressure of 15 mm Hg, renal cortical blood flow decreases approximately 60%, and a reversible 50% drop in urine volume occurs. In contrast, no decrease in urine output occurred when the abdominal wall was lifted with a force of 15 mm Hg during "gasless laparoscopy." It has also been shown that pneumoretroperitoneum, which causes a more gradual increase in intra-abdominal pressure, also caused a more gradual decrease in renal perfusion. Finally, it has been shown that unilateral retroperitoneal insufflation causes decreased renal cortical perfusion of only the ipsilateral kidney if the intra-abdominal pressure is not elevated.

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Chiu AW, Chang LS, Birkett DH. The impact of pneumoperitoneum, pneumoretroperitoneum, and gasless laparoscopy on the systemic and renal hemodynamics. *J Am Coll Surg*. 1995;181:397–406.

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Nishio S, Takeda H, Yokoyama M. Changes in urinary output during laparoscopic adrenalectomy. *BJU Int*. 1999;83:944–947.

C.23. What is the effect of hypercarbia and laparoscopy on the bowel and gastrointestinal system?

Although CO_2 directly causes vasodilatation of the splanchnic capillary beds, the increased intra-abdominal pressure of laparoscopy decreases perfusion, increases systemic vascular resistance, impairs gastric submucosal perfusion and metabolism, and may cause bowel hypoxia at high pressures. On release of intra-abdominal pressure, residual CO_2 again causes vascular dilation, allowing additional CO_2 to enter the blood stream. Myoelectric activity and recovery from ileus is faster after laparoscopic than after open surgery. The combined effect of the increase in abdominal pressure, stretching of the peritoneum by insufflation, and diffusion of CO_2 into bowel is probably responsible for any postoperative nausea.

Bohm B, Milsom JW, Fazio VW. Postoperative intestinal motility following conventional and laparoscopic intestinal surgery. *Arch Surg*. 1995;130:415–419.

Eleftheriadis E, Kotzampassi K, Papanotas K, et al. Gut ischemia, oxidative stress, and bacterial translocation in elevated abdominal pressure in rats. *World J Surg*. 1996;20:11–16.

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Takagi S. Hepatic and portal vein blood flow during carbon dioxide pneumoperitoneum for laparoscopic hepatectomy. *Surg Endosc*. 1998;12:427–431.

C.24. How would you recognize CO_2 embolism during laparoscopy? How does this differ from air embolism? Why should N_2O be discontinued during suspected embolization? Will N_2O increase the size of CO_2 emboli?

Gas embolism can occur whenever the internal pressure of an open vessel is less than the external pressure. Gas embolism may cause increased ventilatory dead space, increased PVR, increased pulmonary artery pressure, and decreased cardiac output. Early signs include a rapid drop in end-tidal CO_2 and Pa_{O_2} and increased Pa_{CO_2}. During laparoscopy, insufflation of a large amount of CO_2 directly into a blood vessel can occur initially after blind Veress needle insertion, especially at high pressures. This should be suspected if the abdominal cavity does not distend equally in all four quadrants despite insufflation of several liters of CO_2. Hypotension, hypoxia, cyanosis, or cardiac arrest can occur. If the gas volume is large enough, a "mill-wheel" murmur may be heard through a precordial or esophageal stethoscope. If ventilation is kept constant, a sudden decrease in end-tidal CO_2 may be noted. The most sensitive means to detect gas emboli are the precordial and transesophageal Doppler and transesophageal echocardiography. Aspiration of foamy blood from a central venous catheter is diagnostic.

CO_2 embolism, however, must be distinguished from air embolism, a far more ominous event, as shown in Table 26.2. CO_2, being extremely soluble in the presence of red blood cells, is much less life threatening than an identically sized intravascular bolus of air. It has been reported that the lethal volume of intravascular CO_2 gas in cats is 30 times greater than the lethal volume of intravascular air.

Air emboli are likely to be entrained in open veins above the level of the heart, a condition that can exist during head and neck or neurosurgery. Other gases that are present, nitrous oxide, for example, will diffuse into that air space according to their diffusion capacities and pressure gradients. Therefore, nitrous oxide will diffuse in, oxygen will be consumed and/or diffuse out, and the size or pressure of the bubble will increase in proportion to the concentration and duration of N_2O being administered, until equilibrium is reached. Eger and Saidman demonstrated that inhalation of 70% N_2O increased the volume of intestinal gas pockets in dogs by twofold in 2 hours, and up to threefold in 4 hours. They calculated that at equilibrium bowel volume could increase up to a maximum of 400%. When N_2O is limited to 50%, however, the size of the gas pocket will not be more than doubled at equilibrium. They also demonstrated that inhalation of 68% to 78% N_2O would cause 300 mL of air in the pleural space to double in volume in 10 minutes and to triple in 45 minutes. A gas bubble composed of 100% CO_2, however, will not enlarge in a patient inhaling 50% or even 75% N_2O because more CO_2 will move out or be absorbed or buffered (also more quickly) than N_2O will move in. This is not to deny that CO_2 gas has caused fatal embolisms or that N_2O should not be discontinued

Table 26.2 Differences Between Air and Carbon Dioxide Emboli

EMBOLISM	AIR	CO_2
Composition	79% N_2, 21% O_2	100% CO_2
Position	Sitting upright	Any
Origin	Vein open to air	No contact with air
Pressure source	Hydrostatic	Insufflator
Solubility	Negligible	Large
Effect of N_2O	Enlarged	Not enlarged

if embolism is suspected. A recent study using transesophageal echocardiography in 16 patients undergoing laparoscopic cholecystectomy reported gas embolism in 11 of the 16 patients (5 during peritoneal insufflation and 6 during gallbladder dissection), but all were subclinical with no signs of cardiorespiratory instability. In addition, conditions for creating CO_2 embolism differ from conditions for air embolism. Other than direct insufflation of CO_2 into a vein, as during Veress needle insufflation, the capillaries and veins within the abdomen are collapsed by the positive pressure within the abdomen, thereby minimizing the chance for CO_2 to enter open vessels.

Derouin M, Couture P, Boudreault D, et al. Detection of gas embolism by transesophageal echocardiography during laparoscopic cholecystectomy. *Anesth Analg*. 1996;82:119–124.

Hong JY, Kim WO, Kil HK. Detection of subclinical CO2 embolism by transesophageal echocardiography during laparoscopic radical prostatectomy. *Urology*. 2010;75(3):581–584.

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Jayaraman S, Khakhar A, Yang H, et al. The association between central venous pressure, pneumoperitoneum, and venous carbon dioxide embolism in laparoscopic hepatectomy. *Surg Endosc*. 2009;23(10):2369–2373.

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Kunkler A, King H. Comparison of air, oxygen, and carbon dioxide embolization. *Ann Surg*. 1959;449:95–99.

C.25. What is the mechanism of increase in shunting resulting from embolization?

Emboli in the pulmonary capillaries cause an increase in PVR (vasoconstriction), which leads to increased pulmonary artery, right ventricle, and right atrium pressures and opening of pulmonary precapillary arteriovenous anastomoses, resulting in shunt and hypoxemia.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 6th ed. Philadelphia: Butterworth-Heinemann; 2005:116.

C.26. How is gas embolism (CO_2 or air) treated?

- Nitrous oxide should be discontinued, and the FIO_2 should be increased to 1.0.
- Identify and occlude the air entrainment site. Insufflation (in the case of CO_2) should be halted, and the pneumoperitoneum should be released immediately.
- An increase in the rate and volume of controlled ventilation with PEEP has been suggested as a method of minimizing air entrainment. However, this may decrease the cardiac output and excessively increase the airway pressure and PVR, and can lead to paradoxical air embolization.
- If possible, the patient should be placed in steep left lateral decubitus Trendelenburg position to prevent obstruction of the pulmonary outflow tract and right ventricular failure.

- A CVP catheter is useful for diagnosis and for therapeutic aspiration of air. Radial artery cannulation is useful to track improvement or deterioration.
- Therapy is essentially supportive and may include fluids, vasopressors, and pulmonary arterial catheterization. A large bolus of gas may form a gas lock in the right atrium, decreasing the cardiac output. Smaller bubbles can lodge in the lungs, causing pulmonary hypertension, right ventricular failure, and pulmonary edema. Venous gas emboli may also enter the arterial circulation through an atrial septal defect or open foramen ovale, a condition that may exist in 20% of patients.

Beck DH, McQuillan PJ. Fatal carbon dioxide embolism and severe haemorrhage during laparoscopic salpingectomy. *Br J Anaesth.* 1994;72:243–245.

Gravenstein N, ed. *Manual of Complications During Anesthesia.* Philadelphia: JB Lippincott; 1991:332–345.

C.27. What are the causes of pneumothorax or pneumomediastinum during laparoscopy? How would you diagnose it? How would you treat it?

Pneumothorax can result from migration of the laparoscopic gas under pressure or from direct pulmonary barotrauma.

During laparoscopy, CO_2 under pressure can pass from the abdominal cavity into the pleural and pericardial spaces through anatomic or congenital paths (e.g., the hiatus around the esophagus) or through acquired defects in the diaphragm. (Embryologically, before formation of the diaphragm, the peritoneal and pleural cavities derived from one sac.) CO_2 gas insufflated retroperitoneally gains rapid direct access to a vast space, and may result in widespread subcutaneous emphysema.

Pneumothorax can be diagnosed by a sudden decrease in pulmonary compliance, an increase in airway pressure, an increase in $P_{ET}CO_2$ and P_{aCO_2}, an unchanged or decreased P_{aO_2}, an unchanged or decreased BP, abnormal motion of the involved side hemidiaphragm, and absence of breath sounds without wheezing on the affected side. The shape of the capnogram usually is unchanged. Fiberoptic bronchoscopy will rule out endobronchial intubation, and intraoperative chest fluoroscopy or x-ray film will confirm the diagnosis.

Pneumothorax caused by laparoscopic gas is easily treated or it can resolve spontaneously. One study reports an incidence of pneumothorax in 7 of 46 patients undergoing laparoscopic fundoplication for repair of hiatus hernia. In these cases, intraoperative treatment consisted of PEEP and increased minute ventilation to reinflate the lung and increased pressure to decrease the gradient from abdomen to pleural cavity and possibly to seal the tear.

Alternatively, pneumothorax may be undetected until the patient wakes up and exhibits respiratory distress and restlessness, which can be misinterpreted as pain or inadequate reversal of the muscle relaxant. Treatment consists of 100% oxygen by mask. CO_2 will quickly diffuse out, as can be easily seen by serial blood gases and x-ray films, and invasive treatment is unnecessary.

Because of the increased volumes and pressures in the lung during laparoscopy, pneumothorax can also result from barotrauma. This cause of pneumothorax is far more serious and may require tube thoracostomy. Attempts at hyperventilating to decrease the $P_{ET}CO_2$ can result in overdistention and rupture of alveoli, with subsequent dissection of the anesthetic gases into the perivascular sheaths, mediastinum, pleura, and fascial planes of the head and neck. Large tidal volumes and rapid ventilator rates can be especially dangerous in patients with COPD or bullae because insufficient emptying time may increase air trapping.

Bartelmaos T, Blanc R, DeClaviere G, et al. Delayed pneumomediastinum and pneumothorax complicating laparoscopic extraperitoneal inguinal hernia repair. *J Clin Anesth.* 2005;17:209–212.

Batra MS, Driscoll JJ, Coburn WA, et al. Evanescent nitrous oxide pneumothorax after laparoscopy. *Anesth Analg.* 1983;62:1121–1123.

Joris JL, Chiche J-D, Lamy ML. Pneumothorax during laparoscopic fundoplication: diagnosis and treatment with positive end-expiratory pressure. *Anesth Analg.* 1995;81:993–1000.

Streich B, Decailliot F, Perney C, et al. Increased carbon dioxide absorption during retroperitoneal laparoscopy. *Br J Anaesth.* 2003;91:793–796.

C.28. How would you decide when to extubate?

In addition to the usual criteria for extubation, prolonged laparoscopy in the Trendelenburg position requires other considerations.

Delay extubation if the patient has edema, venous congestion, and duskiness of the head and neck. Sometimes the tongue becomes edematous. If unsure, check the eyes for periorbital, conjunctival, or lid edema, and keep the patient in head-up position until the conjunctivae no longer seem raised or watery.

Causes of edema include dependent stasis from the Trendelenburg position, resistance from elevated abdominal and thoracic pressures, and temporary fluid overload from oliguria or anuria. In some cases it is best to leave the patient intubated until diuresis has begun, especially because PACU pulmonary edema is not rare.

D. Postoperative Management

D.1. What are some of the unique complications of laparoscopy?

Injuries from instruments

Improper placement of Veress needle or trocars can cause abdominal wall bleeding, blood vessel or visceral puncture, subcutaneous emphysema, peritonitis, wound infections, hernia at the trocar site, and hemorrhage. Thermal injuries may occur from cautery or laser use. Staples and clips can cause nerve entrapment.

Complications of pneumoperitoneum

Increased intra-abdominal pressure can result in bowel ischemia, omental or bowel herniation, gastric regurgitation, excessive compression of vena cava, decreased venous return, venous stasis in legs, hypotension, increased intrathoracic pressure, mediastinal and subcutaneous emphysema, pneumothorax, barotrauma, CO_2 gas embolism, atelectasis, nausea and vomiting, bradyarrhythmias from vagal stimulation of trocar insertion and peritoneal distention, dysfunction of ventriculoperitoneal shunts, and referred shoulder pain from CO_2 gas retained under the diaphragm.

Systemic effects of CO_2 absorption

Among the systemic effects of CO_2 absorptions are hypercarbia, acidosis, increased sympathoadrenal stimulation, hypertension, tachycardia, increased intracranial pressure, embolization, and sickle cell crisis. Arrhythmias can occur from hypercarbia, hypoxia, and catecholamines and in combination with halothane.

Trendelenburg position

Venous congestion of head and neck, increased venous pressure, increased intracranial pressure, retinal hemorrhage, retinal detachment, increased intraocular pressure

and glaucoma attack, endobronchial intubation and hypoxemia, ventilation–perfusion mismatch and hypoxia, neuropathy, corneal and conjunctival edema, edema of airway including larynx, airway obstruction and closure, brachial plexus injury from shoulder braces, femoral nerve and peroneal neuropathies, and an assortment of respiratory complications have been reported with use of the Trendelenburg position.

Late complications

Among the late complications are bowel obstruction from injury, cautery burn, intestine or omentum herniation through the trocar site, adhesions, deep vein thrombosis, and nerve injury resulting from improper padding. Fever may indicate infection from bowel necrosis. Cutaneous metastasis can occur at the port site.

Awad H, Santilli S, Ohr M, et al. The effects of steep Trendelenburg positioning on intraocular pressure during robotic radical prostatectomy. *Anesth Analg.* 2009;109(2):473–478.

Bangma CH, Kirkels WJ, Chadha S, et al. Cutaneous metastasis following laparoscopic pelvic lymphadenopathy for prostatic carcinoma. *J Urol.* 1995;153:1635–1636.

Bolder PM, Norton ML. Retinal hemorrhage following anesthesia. *Anesthesiology.* 1984;61:595–597.

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Fuller J, Ashar BS, Carey-Corrado J. Trocar-associated injuries and fatalities: an analysis of 1399 reports to the FDA. *J Minim Invasive Gynecol.* 2005;12:302–307.

Joshi GP. Complications of laparoscopy. *Anesthesiol Clin North America.* 2001;19:89–105.

Miele VJ, Bendok B, Bloomfield SM. Ventriculoperitoneal shunt dysfunction in adults secondary to conditions causing a transient increase in intraabdominal pressure: report of three cases. *Neurosurgery.* 2004;55:434.

Nishikawa K, Nagashima C, Shimodate Y, et al. Migration of the endotracheal tube during laparoscopy-assisted abdominal surgery in young and elderly patients. *Can J Anaesth.* 2004;51:1053–1054.

Santana A, Crausman RS, Dubin HG. Late onset of subcutaneous emphysema and hypercarbia following laparoscopic cholecystectomy. *Chest.* 1999;115:1468–1471.

Sharma A, Berkeley A. Intraoperative drug-eluting stent thrombosis in a patient undergoing robotic prostatectomy. *J Clin Anesth.* 2009;21(7):517–520.

D.2. What postoperative orders will you write? When would you remove the Foley catheter and arterial line? Under what circumstances would you order a chest x-ray film?

Immediate chest x-ray film is ordered if respiratory distress, subcutaneous emphysema, and actual or suspected pneumothorax occurred; the case was prolonged and retroperitoneal; the patient was oliguric despite adequate hydration; intra-abdominal pressure was greater than 15 mm Hg; or the patient has a history of cardiac or pulmonary disease.

Do not remove the arterial line until the patient is stable and blood gas values are normal. Check urine volumes. Expect an immediate diuresis. Do not remove the Foley catheter until the patient is stable, with fluid intake and volume output stable. Order IV fluids. Check voiding after the catheter is removed. Appropriate medications for nausea and pain control must be written. Ketorolac may be given if the surgeon agrees and if there is no contraindication. Patient-controlled analgesia usually is not

necessary. For ambulatory patients, an adult escort must be available to take them home. Most patients, however, stay overnight.

Pavlin DJ, Chen C, Penaloza DA, et al. Pain as a factor complicating recovery and discharge after ambulatory surgery. *Anesth Analg.* 2002;95:627–634.

D.3. What is the incidence of postoperative nausea and vomiting?

The incidence of nausea and vomiting after laparoscopy has been reported to be as high as 42%. It is the most important factor in causing an overnight admission after ambulatory surgery. IV antiemetics such as ondansetron, often with dexamethasone, may be given, preferably during surgery. The cause of nausea and vomiting is believed to be rapid peritoneal distention. Neurogenic pathways are activated by traction reflexes and by splanchnic pressure and manipulation.

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SECTION VII

The Reproductive System

CHAPTER 27

Placenta Previa/Placenta Accreta

Jill Fong

A 41-YEAR-OLD WOMAN

gravida 4 para 3, is electively scheduled for her third cesarean section at 36 weeks of gestation. She has placenta previa which was diagnosed by sonography after a single episode of painless vaginal bleeding at 28 weeks of gestation which resolved spontaneously. Her vital signs are as follows: blood pressure, 110 per 56 mm Hg; heart rate, 85 beats per minute; respiratory rate, 22 breaths per minute; and oxygen saturation (Spo_2) 98% on room air. Her hematocrit is 35%.

A. Medical Disease and Differential Diagnosis

1. What are the leading causes of maternal mortality, and what role does anesthesia play in this mortality?
2. What is the differential diagnosis for an antepartum hemorrhage?
3. How would you diagnose the etiology of antepartum bleeding?
4. What is the incidence of placenta previa, and what are the associated conditions?
5. What are the different types of placenta previa?
6. What is the usual obstetric management for placenta previa?
7. What is vasa previa? How is it diagnosed and managed?
8. What are the risk factors for the development of a placental abruption?
9. How is placental abruption diagnosed and managed?
10. What complications are associated with placental abruption?

11. Who is at risk for uterine rupture, and how is uterine rupture diagnosed?
12. What is the treatment for uterine rupture?
13. Is this patient at risk for postpartum bleeding?
14. What are the different types of placenta accreta?
15. How is placenta accreta diagnosed?
16. How is placenta accreta managed obstetrically?
17. Is an evaluation for fetal lung maturity indicated in this patient before cesarean section, and how is fetal lung maturity evaluated?

B. Preoperative Evaluation and Preparation

1. How does pregnancy change respiratory function, and what impact does this have on anesthetic care?
2. What are the maternal cardiovascular changes of pregnancy?
3. What are the maternal gastrointestinal changes of pregnancy?
4. What hematologic changes occur during pregnancy?
5. What laboratory data do you need before taking this patient to the operating room?
6. What preoperative medications would you administer to this patient?

C. Intraoperative Management

1. What monitors would you use for this patient?
2. What anesthetic could be used in this patient?
3. What are the absolute and relative contraindications for neuraxial anesthesia?
4. What is the usual amount of blood loss expected with delivery?
5. What are the physical findings associated with blood loss?
6. How is postpartum hemorrhage defined, and what are the etiologies of this bleeding?
7. After delivery of the fetus, the placenta is removed with some difficulty in one small area and generalized oozing from the placental implantation site is noted. What is the most likely cause of this patient's bleeding?
8. After delivery of the placenta in a cesarean section, what maneuvers and drugs can enhance myometrial contractility and therefore, decrease blood loss?
9. If this patient had ongoing bleeding intraoperatively, what guidelines help determine when red blood cell (RBC) transfusions should be given?
10. If this patient had a massive blood loss, what blood replacement therapy would be indicated?
11. What is the role of type O Rh-negative (universal donor) un-crossmatched blood in emergency transfusions, and how does this change your future management?
12. What complications can occur from the transfusion of blood products?
13. What is the role of autologous transfusion in obstetric patients?
14. Significant intraoperative blood loss required the transfusion of 8 units of type-specific, crossmatched packed RBCs (pRBCs). This patient had generalized oozing in the surgical field and hematuria. What is your differential diagnosis?
15. What is disseminated intravascular coagulation (DIC)?
16. What is the role of recombinant activated factor VII (rFVIIa) in obstetric patients?
17. What laboratory tests should be ordered during the resuscitation of this patient?
18. Define amniotic fluid embolism (AFE) and discuss treatment.

D. Postoperative Management

1. If the patient received epidural anesthesia and subsequently developed disseminated intravascular coagulation (DIC), when should the epidural catheter be removed?
2. You have successfully treated the patient's massive hemorrhage. Her laboratory values have returned to normal. Her central venous pressure (CVP) is within normal limits and urine output is appropriate. The patient, however, is still hypotensive despite appropriate intravascular volume replacement and support with vasopressors. What is your concern in this case?

A. Medical Disease and Differential Diagnosis

A.1. What are the leading causes of maternal mortality, and what role does anesthesia play in this mortality?

The maternal mortality ratio (MMR) is defined as the number of maternal deaths per 100,000 maternities. The exact definitions of "maternal" death and "maternities" are defined differently by the different agencies collecting the statistics. Developed versus developing countries have a markedly different incidence of maternal death; 99% of maternal deaths occur in developing countries. According to the World Health Organization in 2005, there were 400 maternal deaths per 100,000 live births globally. The MMR's were 9 and 450 for developed and developing regions, respectively. In developing countries, the leading causes of death are hemorrhage, hypertensive disorders of pregnancy, and sepsis. Obstetric hemorrhaging is the single most important cause of maternal mortality worldwide and accounts for almost half of all postpartum deaths. Anemia, obstructed labor, HIV/AIDS, and unsafe abortions also play a role. Early marriage (a girl <18 years old) is a major health risk for girls; for girls, ages 15 to 19, pregnancy is the leading cause of death worldwide. Women in their 20s are 5 times less likely to die in childbirth than girls less than 15 years old. In developed countries, hypertensive disorders of pregnancy, embolic disorders, and hemorrhage account for slightly less than 50% of maternal deaths; 14% are attributed to indirect deaths due most commonly to cardiovascular disease. In the United States, based on data from the Pregnancy Mortality Surveillance System of the Centers for Disease Control and Prevention, hemorrhage directly caused more than 17% of 4,200 pregnancy-related maternal deaths. Clark and coworkers found that 12% of maternal deaths were caused by obstetric hemorrhage in a report from the Hospital Corporation of America. In the United Kingdom, the Confidential Enquiry into Maternal and Child Health found that hemorrhage was a major factor in maternal deaths.

In developed regions, the estimated anesthesia-related MMR ranges between 1 to 3 deaths per 1,000,000 live births. If a maternal death can be attributed to an anesthetic complication and if an ideal anesthetic would have likely avoided this death, the death is considered anesthetic-related. For cesarean section, general anesthesia probably continues to be more hazardous than neuraxial anesthesia.

Berg CJ, Chang J, Callaghan WM, et al. Pregnancy-related mortality in the United States, 1991–1997. *Obstet Gynecol.* 2003;101:289–296.

Chestnut DH, Polley LS, Tsen LC, et al., eds. *Chestnut's Obstetric Anesthesia: Principles and Practice.* 4th ed. Philadelphia: Mosby; 2009:853–862.

Clark SL, Belfort MA, Dildy GA, et al: Maternal death in the 21st century: causes, prevention, and relationship to cesarean delivery. *Am J Obstet Gynecol.* 2008;199:36.e1–e5.

Cunningham FG, Leveno KJ, Bloom SL, et al., eds. *Williams Obstetrics.* 23rd ed. New York: McGraw-Hill; 2010:4–7.

Gerberding JL: Centers for Disease Control and Prevention: Update: pregnancy-related mortality ratios, by year of death—United States, 1991–1999. *MMWR.* 2003;52:1.

Lalonde A, Daviss BA, Acosta A, et al: Postpartum hemorrhage today: ICM/FIGO initiative 2004–2006. *Int J Gynaecol Obstet*. 2006;94(3):243–253.

McCormick ML, Sanghvi HC, Kinzie B, et al. Preventing postpartum hemorrhage in low-resource settings. *Int J Gynaecol Obstet*. 2002;77(3):267–275.

Mhyre JM, Riesner MN, Polley LS, et al. A series of anesthesia-related maternal deaths in Michigan, 1985–2003. *Anesthesiology*. 2007;106:1096–1104.

World Health Organization. Maternal Mortality in 2005: estimates Developed by WHO, UNICEF, and UNFPA. Geneva: Department of Reproductive Health and Research; 2007.

A.2. What is the differential diagnosis for an antepartum hemorrhage?

Antepartum hemorrhage typically refers to uterine bleeding after 20 weeks of gestation that is unrelated to labor and delivery. Four to five percent of pregnancies are complicated by antepartum hemorrhage. The most common causes of antepartum hemorrhage are placenta previa and placental abruption. Antepartum bleeding generally poses a greater threat to the fetus than the mother. Placenta previa is the abnormal implantation of the placenta over or adjacent to the cervical os and in front of the fetal presenting part. *Placental abruption*, or abruptio placentae, refers to the premature separation of a normally implanted placenta from the uterus' decidua basalis before delivery of the fetus.

Rare causes of antepartum bleeding include velamentous insertion of the umbilical cord with the involved placental vessels overlying the cervix, which is known as vasa previa, uterine rupture, cervicitis, and local genital tract lesions.

In the remaining cases, it is not always possible to identify the source of antepartum bleeding. Usually, this type of bleeding begins with minimal symptoms, if any, and stops; no anatomic cause is identified at delivery, and it is likely attributable to marginal placenta separation. However, these pregnancies have a higher risk of poor neonatal outcome and preterm delivery.

Ajayi RA, Soothill PW, Campbell S, et al. Antenatal testing to predict outcome in pregnancies with unexplained antepartum haemorrhage. *Br J Obstet Gynaecol*. 1992;99:122.

Cunningham FG, Leveno KJ, Bloom SL, et al., eds. *Williams Obstetrics*. 23rd ed. New York: McGraw-Hill; 2010:758.

Leung TY, Chan LW, Tam WH, et al. Risk and prediction of preterm delivery in pregnancies complicated by antepartum hemorrhage of unknown origin before 34 weeks. *Gynecol Obstet Invest*. 2001;52:227.

McCormack RA, Doherty DA, Magann EF, et al. Antepartum bleeding of unknown origin in the second half of pregnancy and pregnancy outcomes. *BJOG*. 2008;115(1):1457.

A.3. How would you diagnose the etiology of antepartum bleeding?

With antepartum bleeding, digital examination of the cervix *should be avoided* until the diagnosis of placenta previa has been excluded because digital examination of a placenta previa can cause immediate, severe hemorrhaging. Classically, it has been taught clinically that painless uterine bleeding is indicative of placenta previa, while painful uterine bleeding signifies placental abruption. The differential diagnosis, however, is not actually that straightforward; for instance, labor or placental separation accompanying a previa may cause pain, whereas pain from an abruption may mimic normal labor. Transabdominal sonography is a simple and safe method of locating the placenta in a suspected placenta previa. Transvaginal sonography has been shown to be superior to transabdominal sonography and is currently the imaging modality of choice. Recently, transperineal sonography has been shown to have a 98% positive-predictive value and 100% negative-predictive value of placenta

previa. On the other hand, sonography infrequently aids in the diagnosis of an acute placental abruption because fresh clot and placenta appear sonographically similar. Negative findings on sonographic examination do not rule out a placental abruption. Magnetic resonance imaging (MRI) has been used by numerous investigators to visualize placental abnormalities, including placenta previa, but is unlikely to replace sonography any time soon due to availability and cost limitations.

Based on the accuracy and safety of transvaginal sonography in detecting placental position, the "double setup" is rarely, if ever, used. The double setup was a vaginal examination done in an operating room with the patient and medical personnel completely prepared to do an emergency cesarean section if hemorrhaging should occur.

Fleischer AC, Manning FA, Jeanty P, et al., eds. *Sonography in Obstetrics and Gynecology: Principles and Practice*. 5th ed. Stamford, CT: Appleton & Lange; 1996:720.

Glantz C, Purnell L. Clinical utility of sonography in the diagnosis and treatment of placental abruption. *J Ultrasound Med*. 2002;21(8):837–840.

Rani PR, Haritha PH, Gowri R. Comparative study of transperineal and transabdominal sonography in the diagnosis of placenta previa. *J Obstet Gynaecol*. 2007;33(3):134–137.

A.4. What is the incidence of placenta previa, and what are the associated conditions?

The incidence of placenta previa in the United States is about 1 in 300 deliveries. The risk of having placenta previa increases with advancing maternal age, multiparity, multifetal gestations, previous cesarean delivery, prior uterine surgery, cigarette smoking, cocaine use, and unexplained increases in maternal serum alpha-fetoprotein levels. Sanderson and Milton found that 12% of placentas were "low lying" at 18 to 20 weeks. As pregnancy progressed, more than 90% of these "low-lying" placentas move away from the cervix and out of the lower uterine segment. If the internal os was not covered, none of these patients had a placenta previa or bleeding. If the internal cervical os was partially covered by placenta at midpregnancy, approximately 40% persisted as a previa. After sonographic identification of a placenta previa before 28 weeks gestation, the likelihood that the previa persists is greater in prior cesarean section patients.

Placenta previa is associated with an increased risk of antepartum bleeding, intrapartum and postpartum hemorrhage, abnormalities of placental adherence, hysterectomy, blood transfusions, preterm birth with perinatal morbidity and mortality, congenital malformations, septicemia, and thrombophlebitis. Zaki et al. found that 10% of 112 consecutive placenta previa cases had an associated placenta accreta. Additionally, in the presence of a prior cesarean section, the patient with placenta previa is at greater risk for having a placenta accreta; this risk increased as the number of cesarean sections increased. The association between placenta previa and placenta accreta with its abnormally firm uterine attachment of the placenta might be due to poor development of the decidua in the lower uterine segment.

Crane JM, Van den Hof MC, Dodds L, et al. Maternal complications with placenta previa. *Am J Perinatol*. 2000;17:101–105.

Crane JM, Van den Hof MC, Dodds L, et al. Neonatal outcomes with placenta previa. *Obstet Gynecol*. 1999;93:541–544.

Cunningham FG, Leveno KJ, Bloom SL, et al., eds. *Williams Obstetrics*. 23rd ed. New York: McGraw-Hill; 2010:769–774.

Oyelese Y, Smulian JC. Placenta previa, placenta accreta, and vasa previa. *Obstset Gynecol*. 2006;107:927–941.

Sanderson DA, Milton PJD. The effectiveness of ultrasound screening at 18–20 weeks gestational age for predication of placenta previa. *J Obstet Gynaecol*. 1991;11:320.

Zaki ZM, Bahar AM, Ali ME, et al. Risk factors and morbidity in patients with placenta previa accreta compared to placenta previa non-accreta. *Acta Obstet Gynecol Scand*. 1998;77(4):391–394.

A.5. What are the different types of placenta previa?

Placenta previa is a term used to describe a placenta that is implanted over or very near the internal cervical os with classifications based on the degree to which the os is covered. Normally, the placenta implants in the upper uterine segment, but in placenta previa the placenta totally or partially implants in the lower uterine segment. If the placenta completely covers the internal os, it is a total placenta previa. A partial placenta previa covers only part of the os, while the placenta in a marginal placenta previa just reaches the os and covers only the margin of the internal os. This differs from a low-lying placenta, which is implanted in the lower uterine segment but does not reach the os. In vasa previa, the fetal vessels course through the membranes and cover the internal cervical os.

Cunningham FG, Leveno KJ, Bloom SL, et al., eds. *Williams Obstetrics*. 23rd ed. New York: McGraw-Hill; 2010:769.

A.6. What is the usual obstetric management for placenta previa?

Obstetric management of placenta previa patients depends upon whether the fetus is preterm with no other indications for delivery, the fetus is reasonably mature, labor has begun, or hemorrhage is so severe as to mandate delivery despite gestational age. With many previas, the first episode of bleeding usually begins without warning or pain, stops spontaneously, and, fortunately, rarely causes maternal or fetal compromise. A mature fetus with or without labor should be delivered. With a preterm fetus and no persistent active uterine bleeding, management consists of close observation for bleeding and activity restriction in an inpatient setting or, in certain selected patients, an outpatient setting. The goal of this expectant management is to delay delivery until the fetus is mature. Maternal vital signs and hemoglobin (Hgb) are checked at regular intervals depending on when the bleeding, if it exists, subsides. Fetal well-being also is assessed regularly. Fetal maturity is done as indicated. Between 24 and 34 weeks of gestation, betamethasone, a corticosteroid, often is given to the patient with placenta previa to accelerate fetal lung maturity. In previa patients with preterm labor, tocolytic therapy may be used to prolong gestation if both the mother and fetus are stable.

As gestational age increases, there is an increased risk of significant bleeding that would necessitate delivery. It is, therefore, preferable to perform a cesarean delivery under controlled, non-emergent conditions. After documenting fetal lung maturity by amniocentesis at 36 to 37 weeks of gestation, an elective cesarean section can be done at this time. If lung maturity does not exist, an elective cesarean should be done at 38 weeks without another amniocentesis. The necessity of fetal lung maturity testing in relation to exact gestational age and the timing of delivery varies slightly between obstetricians. Patients with placenta previa almost always are delivered by cesarean section. When the placenta is greater than 2 cm away from the cervical os, however, small studies suggest that vaginal delivery may be safe. Normally, with placenta removal, the myometrium of the uterus contracts and re-establishes vascular integrity by constricting the open vessels in the placental bed. In patients with placenta previa, bleeding after placenta removal can be brisk because the lower uterine segment contracts poorly and therefore, does not constrict the avulsed vessels. There is a known association between placenta previa and placenta accreta that may further exacerbate uterine bleeding and require additional surgical and/or radiologic interventions to staunch the bleeding.

As needed, adequate intravenous access and laboratory studies, including a complete blood count, coagulation profile, and a type and screen/crossmatch should be obtained as circumstances dictate. Rh (anti-D) immune globulin should be administered to Rh-negative women with an acute bleeding episode, and a Kleihauer-Bettke test for quantification of fetal-maternal transfusion should be done to determine if additional immune globulin is required.

Chestnut DH, Polley LS, Tsen LC, et al., eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Mosby/Elsevier; 2009:813.

Cunningham FG, Leveno KJ, Bloom SL, et al., eds. *Williams Obstetrics*. 23rd ed. New York: McGraw-Hill; 2010:769–774.

Oyelese Y, Smulian JC. Placenta previa, placenta accreta, and vasa previa. *Obstet Gynecol*. 2006; 107:927–941.

A.7. What is vasa previa? How is it diagnosed and managed?

Vasa previa refers to intramembranous fetal vessels, unprotected by placenta or umbilical cord, coursing through the membranes over the cervical os and under the fetal presenting part. The incidence is approximately 1 in 2,500 deliveries and associated risk factors include a second trimester low-lying placenta, a placenta with accessory lobes, multiple pregnancies, and pregnancies from in vitro fertilization. An undiagnosed vasa previa is associated with a high fetal mortality (about 60%). Because fetal blood volume is small, any bleeding puts the fetus in jeopardy. When membranes rupture, either spontaneously or artificially, the fetal vessels running through these membranes often rupture. Vaginal bleeding with fetal distress or death when the membranes rupture are seen in an undiagnosed vasa previa and necessitate an emergency cesarean section based on fetal distress. If vaginal blood is present, the presence of fetal (RBCs) can be determined using a Kleihauer-Bettke test or Apt test, although there is rarely time for this. Fortunately, the majority of cases of vasa previa can be diagnosed prenatally by routinely evaluating placental cord insertion by ultrasound examination and transvaginal sonographic color Doppler if the insertion site cannot be delineated clearly. Good outcomes in patients with vasa previa require a prenatal diagnosis and delivery by cesarean section before the membranes rupture.

Oyelese Y, Smulian JC. Placenta previa, placenta accreta, and vasa previa. *Obstet Gynecol*. 2006; 107:927–941.

A.8. What are the risk factors for the development of a placental abruption?

The frequency of placental abruption is about 1 in 200 deliveries. The premature separation of the normally implanted placenta can be total or partial and can lead to external or concealed bleeding. Concealed hemorrhage is associated with greater maternal and fetal risks. The most common conditions associated with placental abruption are gestational hypertension, preeclampsia, and chronic hypertension. The incidence of placental abruption is increased with increased maternal age, high parity, African-American or Caucasian race, prematurely ruptured membranes, cigarette smoking, cocaine use, thrombophilias, leiomyomas, history of previous abruption, and external trauma. The bleeding almost always is maternal because the placental separation is within the maternal decidua.

Cunningham FG, Leveno KJ, Bloom SL, et al., eds. *Williams Obstetrics*. 23rd ed. New York: McGraw-Hill; 2010:761–769.

A.9. How is placental abruption diagnosed and managed?

The signs and symptoms of placental abruption vary considerably. Ultrasonography often does not confirm the diagnosis as the placenta and fresh clots have similar appearances. In severe placental abruptions, the diagnosis often is obvious with fetal distress and demise common. With a live fetus and vaginal bleeding, milder abruptions may be difficult to diagnosis and become a diagnosis of exclusion.

Treatment depends on fetal gestational age and fetal and maternal condition. If the diagnosis is uncertain and the fetus is uncompromised, inpatient expectant management with close observation can be practiced. However, further placental separation can occur at any time and lead to serious fetal compromise or death. Rapid delivery of the compromised, but alive, fetus is by cesarean delivery. If placental separation has led to fetal death, a vaginal delivery usually is preferred; there are two exceptions: a massive hemorrhage that cannot be managed with vigorous blood replacement and obstetric complications that prevent vaginal delivery will necessitate an operative delivery.

Cunningham FG, Leveno KJ, Bloom SL, et al., eds. *Williams Obstetrics*. 23rd ed. New York: McGraw-Hill; 2010:761–769.

A.10. What complications are associated with placental abruption?

Maternal complications with severe abruption can include postpartum hemorrhage, hemorrhagic shock, a consumptive coagulopathy, acute renal failure, and Sheehan syndrome (pituitary failure). Placental abruption can lead to fetal compromise or fetal demise.

Cunningham FG, Leveno KJ, Bloom SL, et al., eds. *Williams Obstetrics*. 23rd ed. New York: McGraw-Hill; 2010:761–769.

A.11. Who is at risk for uterine rupture, and how is uterine rupture diagnosed?

Uterine rupture is typically classified as either complete, with all of the uterine wall layers separated, or incomplete (uterine dehiscence), with the uterine muscle separated but the visceral peritoneum intact. Uterine dehiscence is more common; it is less likely to cause adverse maternal and fetal derangements or necessitate cesarean delivery. The morbidity and mortality rates are higher when the rupture is complete. Prior cesarean delivery is the greatest risk factor associated with uterine rupture. Fortunately, uterine ruptures are rare. Other risk factors associated with uterine rupture include uterine trauma, previous uterine surgery involving the myometrium, a tumultuous labor, midforceps delivery, fetal malpresentation, external and internal version, inappropriate uterotonic medication use, uterine anomalies, placenta increta/percreta, tumors, and uterine over-distention by fetal macrosomia, hydramnios, or multifetal pregnancy. Uterine rupture can be difficult to diagnose because of the varied symptoms and physical findings that can occur. The most consistent sign of uterine rupture is a nonreassuring fetal heart rate pattern. In some patients, the symptoms of uterine rupture will be indistinguishable from those of placental abruption. Other signs that may be present include hypotension, vaginal bleeding, abdominal pain, change in the uterine contour, changes in the uterine contraction pattern, and cessation of labor. There may be little pain, and because most of these ruptures occur during labor, any pain may be masked by the analgesics given to treat the discomfort of labor.

Chestnut DH, Polley LS, Tsen LC, et al., eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Mosby/Elsevier; 2009:817–818.

Cunningham FG, Leveno KJ, Bloom SL, et al., eds. *Williams Obstetrics*. 23rd ed. New York: McGraw-Hill; 2010:573–574, 784–785.

A.12. What is the treatment for uterine rupture?

With a complete uterine rupture, fetal distress and maternal bleeding occur; an emergent cesarean delivery is imperative to deliver the fetus and stabilize the mother. After delivery of the fetus, the uterus can be repaired, the uterine arteries can be ligated, or a hysterectomy can be performed, depending on the size of the rupture and the patient's condition. Fetal distress and/or death are common while maternal death in the developed world is not.

Cunningham FG, Leveno KJ, Bloom SL, et al., eds. *Williams Obstetrics*. 23rd ed. New York: McGraw-Hill; 2010:573–574.

A.13. Is this patient at risk for postpartum bleeding?

Yes, this patient has a higher chance of postpartum bleeding because of her known placenta previa and the increased risk of having an associated placenta accreta. There is a strong association between placenta previa, prior uterine surgery, and placenta accreta. Clark et al. found that placenta previa patients had a 5%, 24%, and 67% risk of having an associated placenta accreta with no, one, and four or more prior cesarean sections, respectively. Similarly, in patients with placenta previa, Silver et al. found a 3%, 11%, 40%, 61%, and 67% incidence of placenta accreta with zero, one, two, three, four, or more prior cesarean sections, respectively.

Clark SL, Koonings PP, Phelan JP. Placenta previa/accreta and prior cesarean section. *Obstet Gynecol*. 1985;66(1):89–92.

Silver RM, Landon MB, Rouse DJ, et al. Maternal morbidity associated with multiple repeat cesarean deliveries. *Obstet Gynecol*. 2006;107(6):1226–1232.

A.14. What are the different types of placenta accreta?

Placenta accreta refers to a placenta that adheres abnormally to the uterus. The normal placenta has three general layers: the decidua, which is maternal in origin and adherent to the uterus; the chorion, including the chorionic villi; and the amnion. Both the chorion and amnion are of fetal origin. Normally, in the first few minutes after delivery of the neonate, the placenta separates from its implantation site at a physiologic cleavage line through the spongy layer of the decidua basalis. In placenta accreta, the decidua basalis is scanty or absent and the placental chorionic villi are attached directly to the uterine myometrium. With placenta increta, the villi invade into the myometrium, and with placenta percreta, the villi penetrate through the myometrium and serosa of the uterus and, sometimes, into adjacent organs. The abnormal adherence may involve the entire placenta (total placenta accreta), several placental lobules (partial accreta), or part or all of a single lobule (focal placenta accreta). The term placenta accreta often is used as a general term to describe all of these conditions.

The incidence of placenta accreta is increasing due mainly to rising cesarean section rates. The incidence was approximately 1 in 2,500 deliveries in the 1980s, 1 in

535 deliveries in 2002, and 1 in 210 deliveries in 2006. Decidual formation is commonly defective over a previous cesarean section scar, in the lower uterine segment, and/or after uterine curettage. Maternal age greater than 35 years, increasing parity, endometrial defects (Asherman syndrome), submucous leiomyomata, and otherwise unexplained elevations in maternal serum alpha-fetoprotein concentration are other risk factors associated with placenta accreta.

Cunningham FG, Leveno KJ, Bloom SL, et al., eds. *Williams Obstetrics*. 23rd ed. New York: McGraw-Hill; 2010:776–780.

Miller DA, Chollet JA, Goodwin TM. Clinical risk factors for placenta previa-placenta accreta. *Am J Obstet Gynecol*. 1997;177:210–214.

Oyelese Y, Smulian JC. Placenta previa, placenta accreta, and vasa previa. *Obstet Gynecol*. 2006;107:927–941.

Wu S, Kocherginsky M, Hibbard JU. Abnormal placentation: twenty year analysis. *Am J Obstet Gynecol*. 2005;192:1458–1461.

A.15. How is placenta accreta diagnosed?

In patients with conditions such as placenta previa and previous uterine surgery that are highly associated with placenta accreta, it is important to have a high index of suspicion and to look carefully for signs of accreta beginning at 20 to 24 weeks of gestation. Prenatal diagnosis of placenta accreta allows for effective planning that helps minimize maternal morbidity. Transabdominal and transvaginal ultrasonography are useful modalities for evaluating placental position and implantation; the loss of the hypoechoic boundary between the placenta and bladder, placental continuity with the bladder wall, and intraplacental sonolucent spaces, venous lakes, or placental lacunae adjacent to the involved uterine wall are strongly suggestive of placenta accreta. The sensitivity and specificity of ultrasound in detecting placenta accreta are approximately 0.77 and 0.96, respectively. Color flow Doppler and MRI can be used as adjunctive diagnostic tools when the diagnosis is uncertain or the placenta is posteriorly placed; they also can help gauge the depth of placental invasion. Although antepartum diagnosis of placenta accreta would be ideal, currently, there is no single diagnostic modality that determines the diagnosis of placenta accreta with absolute accuracy. Unfortunately, the diagnosis of placenta accreta often is made postpartum during the third stage of labor when separation of the placenta does not occur. The first clinical manifestation of placenta accreta is usually profuse, potentially life-threatening bleeding that occurs at the time of attempted manual placental separation. During vaginal delivery, uterine inversion can occur. Placenta accreta has become one of the most common reasons for peripartum hysterectomy.

Oyelese Y, Smulian JC. Placenta previa, placenta accreta, and vasa previa. *Obstet Gynecol*. 2006;107:927–941.

Warshak CR, Eskander R, Hull AD, et al. Accuracy of ultrasonography and magnetic resonance imaging in the diagnosis of placenta accreta. *Obstet Gynecol*. 2006;108:573–581.

A.16. How is placenta accreta managed obstetrically?

Optimal management of placenta accreta has yet to be defined because of the scanty outcome data in the current literature. Prenatal diagnosis and management appear to improve outcome. The problems associated with placenta accreta depend upon the site of implantation, depth of myometrial penetration, and the number of placental lobules involved. Only a focal placenta accreta may not require aggressive surgical intervention. Otherwise, surgical management can be difficult and requires

a multidisciplinary approach in order to minimize maternal complications. If placenta accreta is known to exist antenatally, it is generally accepted that it is ideally treated with an elective cesarean section and hysterectomy; the placenta should be left in place during surgery. The optimal timing for the delivery of the patient with placenta accreta remains controversial. If fetal lung maturity is documented, delivery often is scheduled at 35 to 36 weeks of gestation; some patients with placenta accreta, especially after 35 weeks, will experience hemorrhaging that necessitates immediate delivery. In a retrospective series, Warshak et al. found that patients with a predelivery diagnosis of accreta, who had a planned en bloc hysterectomy without the removal of the placenta at 34 to 35 weeks of gestation after betamethasone administration, had decreased maternal hemorrhagic morbidity and no significant increase in neonatal morbidity. Chestnut et al. found that women having elective peripartum hysterectomies had significantly less intraoperative blood loss, blood transfused, and hypotension than those having emergent obstetric hysterectomies. For women with suspected placenta accreta, some suggest preoperative placement of balloon catheters into the internal iliac arteries. After delivery of the fetus, the catheters may be inflated intermittently during hysterectomy, which may potentially decrease blood loss and provide optimum exposure of the operative field. They also may be used for intraoperative or postoperative embolization of persistent bleeders. The placement of these catheters is not risk free; thrombosis and thromboemboli have been reported. Similarly, some investigators suggest that the placement of preoperative ureteral stents reduced morbidity in cesarean hysterectomies; others use stents intraoperatively as needed.

Because a hysterectomy renders the patient infertile, there has been some interest in attempting to leave the uterus intact. Timmermans et al. reviewed publications using "conservative" management. They found that in some reports, the placenta was partially removed, while in others, it was left intact; some reported the use of methotrexate and/or uterine artery embolization. Overall, 15% of this whole patient population required hysterectomy for hemorrhaging and 3% for infection; approximately 13% of the patients had subsequent pregnancies. They concluded that only in highly select cases when blood loss is minimal and maintenance of fertility is desired can "conservative" management be considered.

Chestnut DH, Dewan DM, Redick LF, et al. Anesthetic management of obstetric hysterectomy: a multi-institutional study. *Anesthesiology*. 1989;70:607–610.

Eller AG, Porter TF, Soisson P, et al. Optimal management strategies for placenta accreta. *BJOG*. 2009;116:648.

Oyelese Y, Smulian JC. Placenta previa, placenta accreta, and vasa previa. *Obstet Gynecol*. 2006;107:927–941.

Timmermans S, van Hof AC, Duvekot JJ. Conservative management of abnormally invasive placentation. *Obstet Gynecol Surv*. 2007;62(8):529–539.

Warshak CR, Ramos, GA, Eskander, R, et al. Effect of predelivery diagnosis in 99 consecutive cases of placenta accreta. *Obstet Gynecol*. 2010;115:65.

A.17. Is an evaluation for fetal lung maturity indicated in this patient before cesarean section, and how is fetal lung maturity evaluated?

Gestational age and fetal lung maturity should be established prior to an elective induction of labor or cesarean delivery before 39 weeks of gestation; ultrasound is used to establish gestational age, and amniotic fluid studies assess fetal pulmonary maturation. Ultrasound documentation of gestational age in the first trimester or early in the second trimester has proven extremely reliable in timing elective inductions or cesarean deliveries. Evaluation for fetal lung maturity is indicated in this patient because both the mother and fetus are stable. If fetal lung maturity is demonstrated, preterm elective scheduling of this patient's delivery is advised

because of the increased risk of bleeding from placenta previa and the danger that this poses to both the mother and fetus. If there was profuse maternal hemorrhaging, fetal maturity would not impact the decision to perform an immediate cesarean delivery.

With the exception of amniotic fluid specimens obtained from the vaginal pool, amniotic fluid analysis obtained by amniocentesis is used to confirm fetal lung maturity. The pulmonary system is one of the last of the fetal organ systems to mature. Respiratory distress syndrome (RDS) is caused by a deficiency of pulmonary surfactant; the surfactant decreases the pressure required to distend the lungs and prevents alveolar collapse. Type II alveolar cells are the major site of surfactant synthesis. Surfactant is packaged in lamellar bodies, discharged into the alveoli, and expelled into the amniotic fluid with pulmonary fluid. Phospholipids make up more than 80% of the surface active material within the lung, and dipalmitoyl lecithin is more than 50% of this phospholipid. Phosphatidylglycerol is the second most abundant lipid in surfactant and significantly improves its properties. There are two types of tests used to determine pulmonary maturity. One type measures the concentration of particular components of pulmonary surfactant, and the other evaluates the surfactant function of these phospholipids. None of the tests perform significantly better than another, and it is recommended that only one test be done. All of the tests are better at predicting the absence, rather than the presence, of respiratory distress developing. *Fluorescence polarization*, the recently modified *TDx-FLM II*, is used by many hospitals as their first-line test of pulmonary maturity; this automated assay measures the surfactant-to-albumin ratio in uncentrifuged amniotic fluid and yields results in approximately 30 minutes. For many years, the labor-intensive *lecithin–sphingomyelin (L/S) ratio* was the gold-standard test. By approximately 32 weeks of gestation, lecithin and sphingomyelin concentrations in amnionic fluid are similar, but after that, the concentration of lecithin compared to sphingomyelin begins to rise. By about 35 weeks of gestation, the L/S ratio is approximately 2.0, and a ratio of 2.0 or greater predicts that 98% of the neonates will not have RDS. *Lamellar body counts* increase with maturity; a count greater than 30,000 to 50,000 per μL is highly predictive of fetal lung maturity. *Phosphatidylglycerol*, which appears after 35 weeks of gestation and increases rapidly between 37 and 40 weeks, can be measured and is an indicator of completed lung maturity. The *foam stability* or *shake test* depends on the functionality of surfactant in amniotic fluid; when amniotic fluid is mixed appropriately with ethanol, the formation of stable foam at the air–liquid interface indicates lung maturity. Other tests exist, and the choice of test should be based upon availability, presence or absence of contaminants, and physician preference.

Neonatal survival increases as birth weight and/or gestational age increases. The use of maternal antenatal steroids and neonatal exogenous surfactant has help decrease neonatal morbidity and mortality. Between 24 and 34 weeks of gestation, a corticosteroid, such as betamethasone, often is given to the parturient with placenta previa to accelerate fetal lung maturity. Infants who are greater than 30 weeks of gestation are not given prophylactic surfactant. These larger neonates, usually greater than 1,250 g, have a lower risk for developing severe RDS, and clinical trials found no benefit in prophylactic versus rescue treatment.

Chestnut DH, Polley LS, Tsen LC, et al., eds. *Chestnut's Obstetric Anesthesia: Principles and Practice.* 4th ed. Philadelphia: Mosby/Elsevier; 2009:750–752.

Escobedo MB, Gunkel JH, Kennedy KA, et al. Early surfactant for neonates with mild to moderate respiratory distress syndrome: a multicenter randomized trial. *J Pediatr.* 2004;144(6):804–808.

Gabbe SG, Niebyl JR, Simpson JL, eds. *Obstetrics–Normal and Problem Pregnancies.* 5th ed. Philadelphia: Churchill Livingstone/Elsevier; 2007:291–292.

B. Preoperative Evaluation and Preparation

B.1. How does pregnancy change respiratory function, and what impact does this have on anesthetic care?

A number of maternal respiratory changes are seen:

- Capillary engorgement of the mucosa is found throughout the respiratory tract, causing swelling of the nasal and oral pharynx, larynx, and trachea; this begins in the first trimester and increases progressively throughout pregnancy.
- By term, there are increases in minute ventilation (45%), tidal volume (45%), and oxygen consumption (30% to 40%); respiratory rate does not change. These changes do not return to their prepregnancy state for at least 6 to 8 weeks after delivery.
- Arterial $Paco_2$ decreases to about 30 mm Hg by 12 weeks of gestation and remains there until it slowly increases after delivery over about 6 to 8 weeks postpartum.
- Arterial pH increases to about 7.44, and there is a partial metabolic compensation for the respiratory alkalosis (HCO_3^- 20 mEq per L).
- Functional residual capacity (FRC) begins to decrease by the fifth month and by term is 20% below prepregnancy values. After delivery, FRC increases and by 1 to 2 weeks postpartum returns to its prepregnant level. Additionally, the supine position will further decrease the FRC to approximately 70% of prepregnant volume.

Capillary engorgement of the airway mucosa necessitates the use of a smaller, 6.0, 6.5, or 7.0 mm, cuffed endotracheal tube in pregnant women. This vascular engorgement results in airway edema and increased airway friability, which may potentially make tracheal intubation more difficult. Because epistaxis is more likely to occur, nasal intubation is relatively contraindicated. Pilkington et al. showed that the number of pregnant women with a Mallampati class IV airway increased 34% between 12 and 38 weeks of gestation. Boutonnet et al. found that the incidence of Mallampati classes III and IV increased during labor when compared to the prelabor period; these changes are not fully reversed by 48 hours after delivery. No predictive factors for the increase in airway class were found; these changes occurred irrespective of any increase in body weight, the duration of first and second stages of labor, or volume of intravenous fluid. Regardless of the cause, difficult and failed intubations are more common in the pregnant than in the nonpregnant population.

The combination of a decreased FRC and increased oxygen consumption make the pregnant patient more susceptible to the rapid onset of hypoxemia in the apneic state. Therefore, before the induction of general anesthesia, the parturient should be "preoxygenated" with 100% oxygen for 3 to 5 minutes while taking normal tidal breaths or, if time is limited, for four vital capacity breaths. This effectively washes nitrogen out of FRC and provides maximal maternal oxygen reserves to allow longer apneic time during tracheal intubation. The reduced FRC combined with the increased minute ventilation increase the rapidity of changes in the depth of anesthesia while employing an inhaled anesthetic technique. In addition, the minimum alveolar concentration (MAC) of inhaled anesthetic agents has been found to be decreased by about 40% in pregnancy.

Benumof JL. Preoxygenation: best method for both efficacy and efficiency. *Anesthesiology.* 1999;91(3):603–605.

Boutonnet M, Faitot V, Katz A, et al. Mallampati class changes during pregnancy, labour, and after delivery: can these be predicted? *Br J Anaesth.* 2010;104(1):67–70.

Chestnut DH, Polley LS, Tsen LC, et al., eds. *Chestnut's Obstetric Anesthesia: Principles and Practice.* 4th ed. Philadelphia: Mosby/Elsevier; 2009:20–21, 28.

Pilkington S, Carli F, Dakin MJ, et al. Increase in Mallampati score during pregnancy. *Br J Anaesth.* 1995;74:638–642.

B.2. What are the maternal cardiovascular changes of pregnancy?

Most cardiovascular changes of pregnancy begin early in the first trimester and peak by 30 to 34 weeks of gestation. At term, the cardiovascular changes include the following:

- Cardiac output increases 40% to 50%. During the first trimester of pregnancy, the cardiac output increases to 40% or 50% above normal and plateaus at approximately 28 weeks of gestation. It remains fairly stable until the stresses imposed by labor increase it further. During labor, cardiac output increases approximately 15% with uterine contractions during the latent phase, 30% in the active phase, and 45% in the expulsive phase when compared to prelabor values. The greatest increase in cardiac output occurs immediately postpartum when it increases an average of 80% above prelabor values. Cardiac output and heart rate decline to prelabor values within 1 hour of delivery. Postpartum, over the next 2 to 4 weeks, cardiac hemodynamic parameters return towards pregravid levels. It can take a year, however, for the residual effects of cardiovascular remodeling to subside.
- Stroke volume increases approximately 30%.
- Heart rate increases to about 15%.
- Systolic blood pressure is minimally affected by pregnancy.
- Diastolic blood pressure decreases up to 20% by midpregnancy, but returns to its prepregnant level at term.
- Systemic vascular resistance decreases 20%.
- CVP remains unchanged.
- Aortocaval compression refers to the gravid uterus compressing the inferior vena cava and/or the abdominal aorta. The extent of the compression depends on the patient's position and weeks of gestation. In the supine position, compression of the inferior vena cava occurs as early as 13 to 16 weeks of gestation. At term in the supine position, the inferior vena cava is occluded almost completely with venous return from the lower extremities occurring through the dilated paravertebral collateral circulation. At term, compression of the aorta also occurs to some degree when supine. Despite this impaired blood flow and concomitant decrease in cardiac output, the majority of supine women are not hypotensive or symptomatic because of the compensatory rise in systemic vascular resistance. However, up to 15% of supine women at term develop supine hypotension syndrome with hypotension, bradycardia, and symptoms of dizziness, lightheadedness, nausea, and even syncope. Aortocaval compression decreases uteroplacental perfusion by decreasing maternal venous return and maternal arterial blood pressure, by compressing the internal iliac arteries, and by obstructing uterine venous drainage which decreases uterine perfusion pressure. For these reasons, all patients after 20 weeks of gestation should be positioned with left uterine displacement.

Chestnut DH, Polley LS, Tsen LC, et al., eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Mosby/Elsevier; 2009:18–23.

Clark SL, Cotton DM, Lee LW, et al. Central hemodynamic assessment of normal term pregnancy. *Am J Obstet Gynecol*. 1989;161(6):1439.

Gabbe SG, Niebyl JR, Simpson JL, eds. *Obstetrics–Normal and Problem Pregnancies*. 5th ed. Philadelphia: Churchill Livingstone/Elsevier; 2007:57–62.

B.3. What are the maternal gastrointestinal changes of pregnancy?

Parturients are considered to be at an increased risk for aspiration of gastric contents. Pregnancy itself does not alter gastric emptying of liquid or solid materials, but during labor, gastric motility does decrease. Gastric acid secretion appears to be unchanged. Because of the upward displacement of the stomach by the gravid uterus, tone in lower esophageal high pressure zone, however, is decreased. This zone normally

prevents the reflux of gastric contents. In the first trimester, the tone in this zone may be unchanged, but in the second and third trimesters, lower esophageal high pressure zone tone falls gradually to about 50% of its preconceptual level. By 36 weeks of gestation, it reaches its lowest point and does not return to prepregnancy levels until 1 to 4 weeks postpartum. As a result, 30% to 50% of women experience heartburn during pregnancy. The increased aspiration risk is thought to be due to the parturient's decrease lower esophageal high pressure zone tone and the increased risk of having difficulty with intubation.

Chestnut DH, Polley LS, Tsen LC, et al., eds. *Chestnut's Obstetric Anesthesia: Principles and Practice.* 4th ed. Philadelphia: Mosby/Elsevier; 2009:23–25, 647.

B.4. What hematologic changes occur during pregnancy?

The hematologic changes seen by term are as follows:

- Intravascular fluid volume increases 45%.
- Plasma volume increases 55%.
- RBC volume increases 30%.

The disproportionate increase in plasma volume compared to RBC volume results in the relative, or physiologic, anemia of pregnancy. By midgestation, hematocrit has typically fallen approximately 15% below prepregnant levels; the Hgb and hematocrit are approximately 11.2 g per dL and 34%, respectively. In late gestation, RBC volume increases, and at term, maternal Hgb and hematocrit are approximately 11.6 g per dL and 35.5%, respectively. This decreased viscosity may aid in maintaining the patency of the uteroplacental vascular bed.

In addition, the following coagulation factors are increased at term: factors I (fibrinogen), VII, VIII, IX, X, and XII. Plasminogen, fibrin degradation products, and fibrinopeptide A are also increased. Factors II and V are unchanged. Factors XI and XIII are decreased as is antithrombin III. Overall, pregnancy is associated with an accelerated, but compensated, rate of intravascular coagulation. Both, the prothrombin time (PT) and activated partial thromboplastin time (aPTT) are shortened 20%, and thromboelastography suggests a hypercoagulable state. The platelet count is typically unchanged at term. However, 0.9% of otherwise normal women will have a platelet count less than 100,000 per mm^3; gestational thrombocytopenia refers to maternal platelet counts of less than 150,000 mm^3 in otherwise normal women.

Chestnut DH, Polley LS, Tsen LC, et al., eds. *Chestnut's Obstetric Anesthesia: Principles and Practice.* 4th ed. Philadelphia: Mosby/Elsevier; 2009:21–23.

B.5. What laboratory data do you need before taking this patient to the operating room?

The laboratory values needed in this healthy parturient having an elective scheduled cesarean section are minimal. A complete blood count with platelets and a type and cross should be sent as this patient is at an increased risk for bleeding and may require the transfusion of blood products. There is no consensus on the type or amount of blood products that should be available. However, many obstetricians and anesthesiologists suggest that at least four units of pRBCs be immediately available with other blood products readily available. Unless the patient has a coagulation disorder or is actively bleeding, a PT, an aPTT, and a fibrinogen level are not needed because the values should be within normal limits.

Chestnut DH, Polley LS, Tsen LC, et al., eds. *Chestnut's Obstetric Anesthesia: Principles and Practice.* 4th ed. Philadelphia: Mosby/Elsevier; 2009:814, 826.

B.6. What preoperative medications would you administer to this patient?

Patients at increased risk for aspiration should receive a nonparticulate oral antacid such as sodium citrate 30 minutes prior to the induction of anesthesia. Intravenous H_2 receptor antagonists, such as ranitidine, and/or metoclopramide may also be given preoperatively for aspiration prophylaxis. This patient is having an elective cesarean delivery and should have a fasting period for solids consistent with the hospital's policy for nonobstetric patients undergoing elective surgery.

American Society of Anesthesiologists Task Force on Obstetric Anesthesia. Practice guidelines for obstetric anesthesia: an updated report by the American Society of Anesthesiologists Task Force on Obstetric Anesthesia. *Anesthesiology.* 2007;106(4): 843–863.

C. Intraoperative Management

C.1. What monitors would you use for this patient?

Standard monitors should be used and include the following: electrocardiogram (ECG), blood pressure cuff, pulse oximeter, end-tidal carbon dioxide monitor, and Foley catheter. In addition, two large-bore intravenous lines, a forced air body warming blanket, intravenous fluid warmers, and intermittent pneumatic compression stockings should be used. If hemorrhaging occurs and urine output falls below 0.5 mL/kg/hour, despite adequate volume replacement, central venous line placement should be considered. A radial arterial line should also be considered if multiple blood samples will be needed and/or hemodynamic instability occurs. Equipment for the rapid infusion of intravenous fluids and blood products should be readily available.

Chestnut DH, Polley LS, Tsen LC, et al., eds. *Chestnut's Obstetric Anesthesia: Principles and Practice.* 4th ed. Philadelphia: Mosby/Elsevier; 2009:814.

C.2. What anesthetic could be used in this patient?

In the patient with placenta previa, a regional or general anesthetic technique could be used. Many anesthesiologists would choose to perform a continuous neuraxial anesthetic in this patient. The choice of anesthetic depends on the cesarean section indication and urgency and the maternal volume status. All patients with placenta previa are at risk for increased intraoperative blood loss due to the poor contractility of the lower uterine segment, the increased risk of an associated placenta accreta, and the possibility of an anterior placenta being cut during uterine incision. Hong et al. prospectively compared epidural to general anesthesia in women undergoing cesarean section for placenta previa. They found that postoperative hematocrits were lower in the patients receiving general anesthesia; there were no group differences with respect to operative times, estimated blood loss, urine output, or Apgar scores. Chestnut et al. found that none of the patients receiving continuous epidural anesthesia for elective or emergency peripartum hysterectomy required an intraoperative induction of general anesthesia in a multi-institutional study. Although these studies looked at epidural anesthesia, options for neuraxial include continuous spinal, combined

spinal-epidural, and continuous epidural anesthesia. Single injection spinal anesthesia can be used, but the unpredictable length of the surgery may make this a poor choice. All patients having neuraxial anesthesia should be informed that if the need arises, general anesthesia may be induced.

If the patient had a known placenta accreta, neuraxial anesthesia could still be used depending upon the urgency of the cesarean section and the maternal volume status. If continuous epidural anesthesia was chosen and internal iliac balloons were to be placed preoperatively to assist with intraoperative hemostasis, the epidural anesthetic could be utilized during their placement. If hemorrhaging occurs intraoperatively and the patient becomes hemodynamically unstable, conversion to general anesthesia may be necessary. This possibility should be discussed with the patient and obstetric team before surgery. On the other hand, if the patient has a suspected placenta percreta, a general anesthetic is the usual choice for the operative cesarean section and hysterectomy because of the extensive surgery that may be required.

If postpartum hemorrhaging occurs, a coordinated team approach aimed at early recognition and treatment is essential. Good communication between *all* the involved specialties is imperative. In Lewis and Drife's report, poor communication between specialties was believed to have been a contributor to maternal death.

Chestnut DH, Dewan DM, Redick LF, et al. Anesthetic management of obstetric hysterectomy: a multi-institutional study. *Anesthesiology.* 1989;70:607–610.

Hong JY, Jee YS, Yoon HJ, et al. Comparison of general and epidural anesthesia in elective cesarean section for placenta previa totalis: maternal hemodynamics, blood loss and neonatal outcome. *Int J Obstet Anesth.* 2003;12:12–16.

Lewis G, Drife J. *Why mothers die 1997–1999–The fifth report of the confidential enquiries into maternal deaths in the United Kingdom.* London: RCOG Press; 2001:134–150.

C.3. What are the absolute and relative contraindications for neuraxial anesthesia?

Absolute contraindications

- Patient inability to cooperate or patient refusal
- Uncorrected maternal hypovolemia or hypovolemic shock
- Infection at the site of needle insertion
- Frank coagulopathies
- Mass lesions causing increased intracranial pressure
- Providers' lack of experience in techniques

Relative contraindications have included maternal systemic infection, neurologic disease, and some isolated blood coagulation test abnormalities. Most cases of properly treated systemic infection or neurologic disease, however, do not currently contraindicate the use of neuraxial anesthesia. Each patient should be treated individually with careful consideration of the benefits and risks of neuraxial anesthesia.

Chestnut DH, Polley LS, Tsen LC, et al., eds. *Chestnut's Obstetric Anesthesia: Principles and Practice.* 4th ed. Philadelphia: Mosby/Elsevier; 2009:431.

C.4. What is the usual amount of blood loss expected with delivery?

The usual amount of delivery-related blood loss depends upon the type of delivery. The average blood loss is 500 mL for a vaginal delivery, 1,000 mL for a cesarean delivery, and 1,500 mL for a cesarean hysterectomy. These values often are underestimated clinically, owing to the significant blood volume expansion that accompanies normal pregnancy.

Pritchard JA, Baldwin RM, Dickey JC, et al. Blood volume changes in pregnancy and the puerperium. II. Red blood cell loss and changes in apparent blood volume during and following vaginal delivery, cesarean section, and cesarean section plus total hysterectomy. *Am J Obstet Gynecol.* 1962;84:1271.

C.5. What are the physical findings associated with blood loss?

The physical findings in relation to percentage of blood loss are listed in Table 27.1.

The effect of blood loss on physical findings reflects the volume deficit, which may not be the same as volume loss. Depending on the nonpregnant blood volume and the corresponding magnitude of pregnancy-induced hypervolemia, a dangerous feature of postpartum bleeding is the failure of the pulse and blood pressure to undergo more than moderate alterations until large amounts of blood (>1,500 mL) have been lost.

Cunningham FG, Leveno KJ, Bloom SL, et al., eds. *Williams Obstetrics.* 23rd ed. New York: McGraw-Hill; 2010:759–761.

Gabbe SG, Niebyl JR, Simpson JL, eds. *Obstetrics–Normal and Problem Pregnancies.* 5th ed. Philadelphia: Churchill Livingstone/Elsevier; 2007:456, 466.

C.6. How is postpartum hemorrhage defined, and what are the etiologies of this bleeding?

In the literature, the definition of postpartum hemorrhage has been variable and has included subjective assessments of blood loss greater than the standard norms (>500 mL for vaginal deliveries and >1,000 mL in cesarean sections), a 10% decline in hematocrit, and/or the need for a blood transfusion. There is no absolute numeric definition of postpartum hemorrhage. The etiologies of postpartum hemorrhage generally can be categorized as those occurring early within 24 hours of delivery and those occurring late from 24 hours until 6 weeks postdelivery. Because the obstetrician typically is faced with early postpartum hemorrhage, the remainder of this discussion will focus on its causes. The two broad etiologies of early postpartum hemorrhage are based on bleeding from the placental implantation site and genital tract trauma. Within the category of placental site bleeding, bleeding is usually due

Table 27.1 The Physical Findings in Relation to Percentage of Blood Loss

BLOOD LOSS	PHYSICAL FINDINGS
<15%–20%	None
20%–25%	Tachycardia (>100 beats/min) and tachypnea
	Narrowed pulse pressure and orthostatic hypotension
	Peripheral vasoconstriction
30%–35%	Worsening tachycardia and tachypnea
	Hypotension
	Oliguria
>40%	Shock
	Altered consciousness
	Anuria

to either myometrial hypotonia, such as that seen with uterine atony and placenta previa, or retained placental tissue as can be seen with invasive placentation such as placenta accreta. Genital tract traumas that lead to postpartum bleeding include genital tract lacerations and uterine rupture. Coagulation defects intensify the bleeding that occurs with any of the above abnormalities.

Cunningham FG, Leveno KJ, Bloom SL, et al., eds. *Williams Obstetrics.* 23rd ed. New York: McGraw-Hill; 2010:759–761.

Gabbe SG, Niebyl JR, Simpson JL, eds. *Obstetrics–Normal and Problem Pregnancies.* 5th ed. Philadelphia: Churchill Livingstone/Elsevier; 2007:466.

C.7. After delivery of the fetus, the placenta is removed with some difficulty in one small area and generalized oozing from the placental implantation site is noted. What is the most likely cause of this patient's bleeding?

The most likely causes of bleeding in this patient are myometrial hypotonia due to the poor contraction of the lower uterine segment and a focal placenta accreta. Near term, at least 600 mL per minute of blood flows through the intervillous space carried by about 120 spiral arteries and their accompanying veins. With placental separation, these vessels are avulsed; hemostasis at the placental implantation site is first achieved by contraction of the myometrium that compresses these relatively large vessels and reestablishes vascular integrity. Subsequently, clotting occurs and the vessel lumens are obliterated. Ineffective myometrial contractions, such as occur with retained placenta or massive blood clots, can impair hemostasis at the implantation site. In this patient, the lower uterine segment, which contains less myometrial tissue, contracts poorly, and hemorrhaging can result despite normal coagulation. Bleeding that occurs after placenta delivery is usually a steady, not a sudden massive, hemorrhage. The constant seepage, however, can lead to an enormous blood loss. Severe postpartum hemorrhage, therefore, can result from uterine atony despite normal coagulation. Conversely, even if coagulation is impaired, vigorous myometrial contraction within and adjacent to the denuded placental implantation site makes severe hemorrhage from this implantation site unlikely. During rapid bleeding, the hematocrit may not accurately reflect the amount of blood lost due to the lack of equilibration with other fluid compartments.

Cunningham FG, Leveno KJ, Bloom SL, et al., eds. *Williams Obstetrics.* 23rd ed. New York: McGraw-Hill; 2010:759–761.

C.8. After delivery of the placenta in a cesarean section, what maneuvers and drugs can enhance myometrial contractility and therefore decrease blood loss?

McCurdy et al. found that spontaneous delivery of the placenta during cesarean delivery reduced blood loss by 30% when compared to manual removal. Manual uterine massage stimulates the myometrium to contract. Uterotonic medications, such as oxytocin, also cause myometrial contractions. Synthetic oxytocin (Pitocin, Syntocinon) is the drug of choice and is given once the fetus is born and the placenta is delivered. Oxytocin increases the frequency and duration of uterine contractions; these contractions are most likely mediated through an increase in intracellular calcium levels. The number of oxytocin receptors in the uterus increases from about 20 weeks of gestation to 34 weeks of gestation, and receptor sensitivity increases during labor. Intravenous therapy is the preferred route of administration, but intramuscular and intrauterine dosing is possible. Initial intravenous treatment usually starts with 20 units of oxytocin

in 1,000 mL of crystalloid solution. Munn et al. found that higher doses (80 units in 500 mL over 30 minutes) were safe, efficacious, and reduced the need for additional uterotonic therapy by 20% when compared with standard dosing of 10 units in 500 mL over 30 minutes. The posterior pituitary produces the polypeptide hormones, oxytocin and antidiuretic hormone. Because they differ from one another by only two amino acids, oxytocin exhibits a small antidiuretic effect that is clinically insignificant unless very large doses are given; in this situation, water intoxication might occur. A bolus of oxytocin can decrease peripheral vascular resistance leading to hypotension that on occasion requires treatment with appropriate vasopressors (ephedrine or phenylephrine). Patients may also exhibit tachycardia and arrhythmias.

When oxytocin fails to produce adequate uterine tone and uterine atony is present, other uterotonic medications should be used. Uterine atony is the most common cause of postpartum hemorrhage and accounts for up to 80% of the cases. The second-line agent chosen depends on its side-effect profile and contraindications. Ergot alkaloids, methylergonovine (Methergine) and ergonovine (ergometrine), are effective uterotonic agents; they are usually given intramuscularly and produce tetanic contractions of the uterus that may be mediated through α-adrenergic receptors. Their usefulness is limited because the induced hypertension, due to vasoconstriction, can be prominent. These agents should be avoided in patients with pre-existing hypertensive disease. Other cardiovascular affects include coronary artery spasm leading to myocardial infarction, arrhythmias, or cerebrovascular accidents. Pulmonary complications have been reported including pulmonary artery vasoconstriction and pulmonary hypertension. Associated side effects include headache, dizziness, nausea, and vomiting.

Prostaglandins are uterotonic agents. The prostaglandins cause an increase in myometrial intracellular calcium levels leading to an increase in myosin light-chain kinase activity and uterine contraction. Intramuscular and intrauterine administration of 15-methyl prostaglandin $F_{2\alpha}$ (Hemabate, carboprost tromethamine) can be used to control of uterine atony. Due to its bronchoconstrictive properties, its use is strongly contraindicated in asthma patients. Rectally administered prostaglandin E_2 (Prostin) is a naturally occurring uterotonic agent that has not been tested in clinical trials for postpartum bleeding, and its unfavorable side effects include fever/chills, nausea/vomiting, diarrhea, and headaches. Finally, Mousa and Alfirevic recently reported that rectally administered misoprostol (Cytotec), a synthetic prostaglandin E_1 analogue, provided no added benefit when compared to standard therapy with oxytocin and ergometrine (ergonovine) in primary postpartum hemorrhage patients.

If pharmacologic methods fail to control atony-related hemorrhage, alternative measures, including uterine tamponade, selective arterial embolization, and surgical intervention must be undertaken.

Cunningham FG, Leveno KJ, Bloom SL, et al., eds. *Williams Obstetrics*. 23rd ed. New York: McGraw-Hill; 2010:399, 775.

de Groot AN, van Dongen PW, Vree TB, et al. Ergot alkaloids: Current status and review of clinical pharmacology and therapeutic use compared with other oxytocics in obstetrics and gynaecology. *Drugs*. 1998;56:523–535.

Gabbe SG, Niebyl JR, Simpson JL, eds. *Obstetrics–Normal and Problem Pregnancies*. 5th ed. Philadelphia: Churchill Livingstone/Elsevier; 2007:330, 468–469.

Izumi H, Garfield RE, Morshita F, et al. Some mechanical properties of skinned fibres of pregnant human myometrium. *Eur J Obstet Gynecol Reprod Biol*. 1994;56:55–62.

McCurdy CM, Magann EF, McCurdy CJ, et al. The effect of placental management at cesarean delivery on operative blood loss. *Am J Obstet Gynecol*. 1992;167(5):1363–1367.

Mousa HA, Alfirevic Z. Treatment for primary postpartum haemorrhage. *Cochrane Database Syst Rev*. 2007;1:CD003249.

Munn MB, Owen J, Vincent R, et al. Comparison of two oxytocin regimens to prevent uterine atony at cesarean delivery: a randomized controlled trial. *Obstet Gynecol*. 2001;98(3):386–390.

C.9. If this patient had ongoing bleeding intraoperatively, what guidelines help determine when red blood cell (RBC) transfusions should be given?

Treatment of serious bleeding demands prompt and adequate refilling of the intravascular compartment. Normovolemia should be maintained, and usually non–dextrose-containing crystalloid solutions are used for the initial volume resuscitation. These solutions rapidly equilibrate into the extravascular space, and therefore, the volume of crystalloid given should be three times as much as the estimated blood loss. Colloid solutions can also be used to maintain normovolemia but confer no greater benefit than crystalloid solutions. Depending on colloid solution (e.g., 5% albumin), the volume that should be administered is the same as that of the estimate blood loss; this may be helpful in facilitating a more rapid repletion of a pre-existing volume deficit.

Defining a universal hematocrit (Hct) or Hgb value below or above which transfusion is either mandatory or contraindicated is difficult. RBCs carry oxygen to the tissues, and the goal of RBC transfusions is to maintain adequate tissue oxygenation. The 2006 American Society of Anesthesiologist Practice Guidelines state that patients with a Hgb concentration $\geq$ 10 g per dL usually do not require RBC transfusion, and if a patient's Hgb concentration is $<$6 g per dL, RBCs should usually be administered. RBC transfusions should be considered in all patients with clinical evidence of inadequate oxygen carrying capacity. In most bleeding obstetric patients, maintaining a Hgb level above 7 g per dL is suggested unless evidence of impaired pulmonary or cardiac function indicates a need for a higher Hgb level.

American Society of Anesthesiologists Task Force on Perioperative Blood Transfusion and Adjuvant Therapies. Practice guidelines for perioperative blood transfusion and adjuvant therapies: an updated report. *Anesthesiology*. 2006;105:198–208.

Silverman JA, Barrett J, Callum JL. The appropriateness of red blood cell transfusions in the peripartum patient. *Obstet Gynecol*. 2004;104:1000–1004.

C.10. If this patient had a massive blood loss, what blood replacement therapy would be indicated?

When blood replacement therapy is indicated, compatible whole blood is ideal for maintaining intravascular volume in the treatment of hypovolemia from catastrophic acute hemorrhage. One unit of whole blood raises the Hct by 3 to 4 volume percent and replaces many coagulation factors, especially fibrinogen. Importantly, using whole blood versus packed red cells and components decreases the exposure of women with severe hemorrhage to blood donors. When whole blood transfusions were compared with packed red cell transfusions or blood product combinations, Alexander et al. reported that the incidence of renal failure, adult RDS, pulmonary edema, hypofibrinogenemia, admission to an intensive care unit, and maternal death decreased significantly in women delivered at Parkland Hospital. However, availability of whole blood is limited; few units of whole blood are kept in the modern blood bank as over 90% of donor blood is fractionated into blood components. For women who do not have massive blood loss, pRBC transfusions are suitable, and component therapy provides better treatment because only the specific component needed is given.

Blood component therapy provides the patient with only the components that they require. The products available are pRBCs, fresh frozen plasma, cryoprecipitate, and platelets. A unit of pRBC is prepared from one unit of whole blood; its plasma is removed and replaced with additives such as citrate, phosphate, dextrose, and adenine. Its volume is about 250 to 325 mL with a hematocrit of 55 to 80 volume percent depending upon the method used for preparation and storage. A unit of pRBCs increases the patient's hematocrit approximately 3 volume percent and Hgb

by about 1 g per dL. Crystalloid infusion and pRBC transfusion are the mainstays of therapy in the bleeding obstetric patient. Fresh frozen plasma (FFP) contains all the necessary coagulation factors, and a unit has a volume of approximately 250 mL. When replacement of coagulation factors is needed for hemostasis as occurs after massive transfusion, FFP transfusion is indicated. In a parturient with surgical bleeding, a fibrinogen level of less than 100 mg per dL, a prolonged PT, and/or a prolonged aPTT are indications for fresh frozen plasma administration in initial doses of 10 to 15 mL per kg. FFP administration is not indicated for hypovolemia. Cyroprecipitate is prepared from FFP and 15 mL contains 200 mg fibrinogen, factor VIII:C, factor VIII:von Willebrand, Factor XIII, and fibronectin. Ten pooled bags (10–15 mL per bag) of cryoprecipitate will increase the fibrinogen level by 65 to 70 mg per dL. In the bleeding obstetric patient, general clotting factor replacement with cryoprecipitate provides no advantage over FFP and should not be used unless volume is problematic or there is a specific factor deficiency. With obstetric hemorrhage, the platelet count should be maintained above 50,000 per mm^3 with the infusion of platelet concentrates. One unit of platelets increases the platelet count 5,000 to 10,000 per mm^3 in an adult woman. A single donor platelet apheresis unit provides the equivalent amount of platelets as six random donor platelet units and should be used if available. Platelets are difficult to store and have a short shelf life (5 days). Typically, the blood bank provides platelets from and ABO- and Rh-compatible donors, but ABO-compatibility is not essential.

Recently, the impact of massive transfusion, defined as 10 or more units of blood with resultant coagulopathy, has been studied by both civilian trauma groups and military combat hospitals. Although replacement therapy with plasma, platelets, and red cells generally should not be based upon any set formula, the results from these studies suggest that patients with severe trauma, massive blood replacement, and coagulopathy have improved survival when the ratio of transfused pRBCs (units) to FFP (units) to platelets (units) approaches 1:1:1. Because there are only a limited number of studies in patients requiring massive transfusion and no data in the obstetric setting, the value of this approach is still controversial and remains to be proven.

Alexander JM, Sarode R, McIntire DD, et al. Use of whole blood in the management of hypovolemia due to obstetric hemorrhage. *Obstet Gynecol.* 2009;113(6):1320–1326.

Cunningham FG, Leveno KJ, Bloom SL, et al., eds. *Williams Obstetrics.* 23rd ed. New York: McGraw-Hill; 2010:791–794.

Santoso JT, Saunders BA, Grosshart K. Massive blood loss and transfusion in obstetrics and gynecology. *Obstet Gynecol Surv.* 2005;60:827–837.

Shaz BH, Dente CJ, Harris RS, et al. Transfusion management of trauma patients. *Anesth Analg.* 2009;108(6):1760–1768.

C.11. What is the role of type O Rh-negative (universal donor) uncrossmatched blood in emergency transfusions, and how does this change your future management?

When typed and screened/crossed blood is unavailable and the hemodynamically unstable, hemorrhaging obstetric patient requires an RBC transfusion in addition to crystalloid and/or colloid solutions, un-crossmatched type O Rh-negative blood can be given. People with type O blood are considered universal donors because they lack A and B antigens, and therefore, their erythrocytes are not hemolyzed by a recipient's anti-A or anti-B antibodies if present. Some type O donors, however, produce high titers of hemolytic anti-A and anti-B antibodies. pRBCs, therefore, are preferable to whole blood because packed erythrocytes have a smaller volume of

plasma and therefore, a minimal amount of anti-A and anti-B antibodies if present. If whole blood is to be used, the blood bank should supply type O blood that is free of anti-A and anti-B antibodies. Some confusion exists as to when it is safe to switch back to the patient's native blood type. After a patient has received two units of type O Rh-negative un-crossmatched whole blood, the patient should not be switched to their type specific (A, B, AB) blood; additional transfusions should be continued with type O blood. The patient must not receive a transfusion of her correct blood type until the blood bank determines that switching back to the patients native blood type is safe. Patients who have received un-crossmatched type O Rh-negative pRBCs can receive many more units without concern for antibody reactions. Individual centers have different policies governing the maximum number of un-crossmatched type O Rh-negative blood units that can be given before switching back to the patient's specific blood type. Most centers do recommend switching to the patient's native blood type as soon as safely possible in order to conserve the emergency supply of type O Rh-negative blood. Recommendations should be received from your local blood bank representative.

Miller RD, Eriksson LI, Fleisher LA, et al., eds. *Miller's Anesthesia.* 7th ed. Philadelphia: Churchill Livingston/Elsevier; 2009:1744–1745.

C.12. What complications can occur from the transfusion of blood products?

Blood transfusion safety has improved over the past several decades. Currently, the most serious and common known risks are administrative errors leading to ABO-incompatible blood transfusion, transfusion-related acute lung injury and infection. Other transfusion-related adverse reactions include delayed hemolytic transfusion reactions, febrile and allergic nonhemolytic transfusion reactions, and transfusion-associated graft-versus-host disease.

The accidental transfusion of ABO-incompatible blood can result in acute intravascular hemolysis. This is typically characterized by the symptoms of fever, chills, nausea, flushing, chest and flank pain, tachycardia, hypotension, DIC, hemoglobinuria, acute renal failure, and potentially death. The rate of such errors in the United States is estimated to be 1 in 14,000 units. Immediate supportive care includes the discontinuation of the transfusion, treatment of the hypotension and hyperkalemia, administration of a diuretic, and urine alkalinization. The unused blood product should be sent back to the blood bank along with a new patient specimen for a second crossmatch. Assays for urine and plasma hemoglobin concentration and a direct antiglobulin antibody screen confirm the diagnosis.

Transfusion-related acute lung injury is a noncardiogenic pulmonary edema that occurs about 6 to 72 hours after transfusion; this life-threatening complication is characterized by severe dyspnea and hypoxia, occurring about 1 in 5,000 transfusions. Its pathogenesis is incompletely understood, but the lung injury appears to involve lipid products from stored components as well as leukocyte reactivity.

The risk of bacterial contamination is less than 1 per million units in the United States, but the transfusion of a contaminated blood component is associated with a high (about 60%) mortality rate making bacterial contamination the leading cause of transfusion-related death. Platelets present the greatest risk of bacterial contamination; the introduction of culture-negative platelets has decreased the risk of an infected platelet transfusion to 1 in 75,000 units.

The use of serologic screening and nucleic acid amplification testing (NAT) on donor blood products have decreased the risk of viral infection transmission. The risk of contracting HIV or hepatitis C is approximately 1 in 2 million units transfused. The risk of *hepatitis B* transmission is estimated to be less than 1 per 200,000 to 500,000

units transfused. The risk of other transfusion-transmitted infectious diseases, such as malaria and cytomegalovirus, is estimated to be less than 1 in 1 million units transfused. However, due to risks to the fetus, pregnant women should receive blood that is seronegative and leukocyte-depleted to further decrease the risk of cytomegalovirus infection. There have been reports of West Nile virus infection and variant Creutzfeldt-Jakob disease acquired via transfusion.

The biochemical changes that occur with the storage of blood can lead to problems in the recipient especially when large amounts are rapidly infused. Hypokalemia, hypocalcemia. and hypothermia can occur and should be promptly corrected.

Chestnut DH, Polley LS, Tsen LC, et al., eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Mosby/Elsevier; 2009:831–832.

Eder AF, Kennedy JM, Dy BA, et al. Bacterial screening of apheresis platelets and the residual risk of septic transfusion reactions: the American Red Cross experience (2004–2006) *Transfusion*. 2007;47(7):1134–1142.

Goodnough LT. Risks of blood transfusion. *Crit Care Med*. 2003;31:S678.

Marik PE, Corwin HL. Acute lung injury following blood transfusion: expanding the definition. *Crit Care Med*. 2008;36(11):3080–3084.

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Stramer SL. Current risks of transfusion-transmitted agents: a review. *Arch Pathol Lab Med*. 2007;131(5):702–707.

C.13. What is the role of autologous transfusion in obstetric patients?

Autologous blood transfusion may avoid the risks of alloimmunization, hemolytic reactions, and viral infections, may potentially decrease the demands on the allogenic blood supply, and may provide a psychological benefit to the patient. There are three methods of autologous transfusion, preoperative (antepartum) donation, normovolemic hemodilution, and intraoperative blood salvage. Each technique may have potential benefits in the properly selected patient population, but applicability is limited and safety anecdotal. Due to the inability to correctly anticipate which patients will require transfusions and the limited amount of transfusable blood obtained, preoperative donation and normovolemic hemodilution are ineffective strategies for avoiding allogenic transfusions in the obstetric patient.

Intraoperative blood salvage has been used in obstetric patients. During cesarean section after placenta delivery, blood is suctioned from the surgical site, collected, and processed through a cell salvage machine that yields a washed, pRBC product for transfusion. There are no prospective randomized studies evaluating the safety of intraoperative blood salvage in obstetrics, but the review of over 400 case reports by Allam et al. did not reveal any complications leading to poor maternal outcome that were directly attributable to the use of this technique. The safety of blood salvage during cesarean section has been questioned because of the theoretical risk of developing an amniotic fluid embolism (AFE); unfortunately, the pathophysiology of AFE is unknown. In the United States, the American Society of Anesthesiologists recommends that "in cases of intractable hemorrhage when banked blood is not available or the patient refuses banked blood, intraoperative cell salvage should be considered if available." Intraoperative blood salvage during cesarean section is more widely accepted in United Kingdom. Leukocyte depletion filters may improve the margin of

safety of the salvaged pRBC product. Because washed pRBCs may contain fetal RBCs, isoimmunization of the mother is possible; anti-D immune globulin should be given when appropriate.

Jehovah's Witness patients have an increased risk of maternal death due to maternal hemorrhage because their religious beliefs prevent them from receiving blood transfusions. In 2004, the society's official magazine, The Watchtower, stated that "Though all witnesses should refuse autologous or heterologous transfusions of blood or one of its major components, the society states that each member should decide for him- or herself whether or not to accept treatment with other blood products like coagulation factors and erythropoietin." The use of intraoperative blood salvage during surgery sometimes is accepted because continuity of the salvaged blood with the patient's circulatory system can be maintained. The exact possibilities for acceptable treatment options should be discussed with each individual patient early in pregnancy.

Allam J, Cox M, Yentis SM. Cell salvage in obstetrics. *Int J Obstet Anesth.* 2008;17:37–45.

American Society of Anesthesiologists Task Force on Obstetric Anesthesia. Practice guidelines for obstetric anesthesia. *Anesthesiology.* 2007;104:869–875.

Catling S. Blood conservation techniques in obstetrics: a UK perspective. *Int J Obstet Anesth.* 2007;16:241–249.

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Massiah N, Athimulams S, Loo L, et al. Obstetric care of the Jehovah's Witness: a 14-year observational study. *Arch Gynecol Obstet.* 2007;279(4):339–343.

Van Wolfswinkel ME, Zwart JJ, Schutte JM, et al. Maternal mortality and serious morbidity in Jehovah's Witnesses in the Netherlands. *BJOG.* 2009;116(8):1103–1108.

Watchtower Bible and Tract Society. Be guided by the living God. *Watchtower.* 2004;15:22–24.

Waters JH, Biscotti C, Potter PS. Amniotic fluid removal during cell salvage in the Cesarean section patient. *Anesthesiology.* 2000;92:1531–1536.

C.14. Significant intraoperative blood loss required the transfusion of 8 units of type-specific, crossmatched packed RBCs (pRBCs). This patient had generalized oozing in the surgical field and hematuria. What is your differential diagnosis?

The obstetric patient can rapidly develop a coagulopathy. It may be a dilutional coagulopathy or DIC. A dilutional coagulopathy can occur when massive blood loss is replaced with crystalloid solutions and pRBCs leading to a relative depletion of platelets and soluble clotting factors. Thrombocytopenia is the most frequent coagulation defect found in women with blood loss and multiple transfusions. Pregnancy-related causes of DIC include hemorrhagic shock, AFE, placental abruption, intrauterine fetal demise, and sepsis due to uterine infection. Additionally, hemolytic transfusion reactions with acute intravascular hemolysis can cause DIC. Acidosis and hypothermia both interfere with the normal functioning of the coagulation system and worsen any coagulopathy.

Chestnut DH, Polley LS, Tsen LC, et al., eds. *Chestnut's Obstetric Anesthesia: Principles and Practice.* 4th ed. Philadelphia: Mosby/Elsevier; 2009:831–832.

Kermode JC, Zheng Q, Milner EP. Marked temperature dependence of the platelet calcium signal induced by von Willebrand factor. *Blood.* 1999;94(1):199–207.

Meng ZH, Wolberg AS, Monroe DM 3rd, et al. The effect of temperature and pH on the activity of factor VIIa: implications for the efficacy of high-dose factor VIIa in hypothermic and acidotic patients. *J Trauma*. 2003;55(5):886–891.

Santoso JT, Saunders BA, Grosshart K. Massive blood loss and transfusion in obstetrics and gynecology. *Obstet Gynecol Surv*. 2005;60:827–837.

C.15. What is disseminated intravascular coagulation (DIC)?

DIC, a consumptive coagulopathy, is a pathologic activation of the coagulation system that occurs in response to a variety of diseases. The process of coagulation is dysregulated and widespread intravascular clotting and resultant bleeding due to the inappropriate consumption of factors and platelets occurs. Thrombi are deposited in the microcirculation and can diminish blood flow to the organs and lead to multisystem organ failure. Simultaneously, increased fibrinolysis occurs with the formation of fibrin degradation products (also called fibrin split products). Once DIC begins, the pathophysiology is the same regardless of the inciting cause. Resolution of DIC requires treatment of the underlying cause. Supportive treatment is aimed at replacing the consumed blood products-"feeding the fire." Laboratory values are indicative of this consumption of clotting products and the increased fibrinolysis that this excess clotting activates and can help guide management. Thrombocytopenia, decreased levels of fibrinogen and coagulation factors, increased levels of fibrin degradation products, increased PT, and increased aPTT are seen.

Cunningham FG, Leveno KJ, Bloom SL, et al., eds. *Williams Obstetrics*. 23rd ed. New York: McGraw-Hill; 2010:785–787.

C.16. What is the role of recombinant activated factor VII (rFVIIa) in obstetric patients?

RFVIIa (NovoSeven), a synthetic vitamin K-dependent glycoprotein was approved by the Food and Drug Administration principally for the treatment of bleeding in individuals with hemophilia A or B, factor VII deficiency, and Glanzmann thrombasthenia. It has been used to facilitate hemostasis in patients bleeding from other coagulopathies, surgery, trauma, and severe obstetric hemorrhage. Use of rFVIIa in obstetrics has been reported in case series and international registries; no randomized controlled trials have been published. At pharmacologic doses, rFVIIa directly activates factor X on the surface of activated platelets at the site of injury independent of tissue factor and factors VIII and IX causing a "thrombin burst" with the conversion of prothrombin into large amounts of thrombin and the local formation of a stable fibrin clot that may control bleeding. Currently, it has not been ruled out that a small amount of tissue factor-dependent activity also might contribute to its hemostatic effect. There are case reports of rFVIIa being used in obstetric cases after massive hemorrhage with symptoms suggesting DIC. Franchini et al. reviewed the literature and found that a median dose of 81.5 μg per kg of rFVIIa has been effective in stopping or decreasing bleeding in 85% of obstetric cases where it has been utilized. Based on personal experience and literature review, they have outlined a treatment scheme for the off-label use of rFVIIa in the treatment of postpartum hemorrhage. They suggest that rFVIIa be considered only after the failure of medical treatment, blood component therapy, and conservative surgical/invasive treatment. Before administering rFVIIa, acidosis, thrombocytopenia, hypofibrinogenemia, hypocalcemia, and hypothermia should be corrected. Then, 90 μg per kg should be given intravenously over 3 to 5 minutes. If no response has occurred 20 minutes later, a second dose of 90 μg per kg should be given. If there is no response after

two doses, hysterectomy should be considered. Because to date all of the information about rFVIIIa in obstetrics is anecdotal, the use of rFVIIa should be determined on an individual case basis. There are unanswered concerns about the increased likelihood of thrombotic events, and the role of rFVIIa remains undefined. The ASA guidelines, however, recommend that rFVIIa administration be considered when "traditional well tested options for treating microvascular bleeding (i.e. coagulopathy) have been exhausted."

American Society of Anesthesiologists Task Force on Perioperative Blood Transfusion and Adjuvant Therapies. Practice guidelines for perioperative blood transfusion and adjuvant therapies: an updated report. *Anesthesiology.* 2006;105:198–208.

Franchini M, Franchi M, Bergamini V, et al. The use of recombinant activated FVII in postpartum hemorrhage. *Clin Obstet Gynecol.* 2010;53(1):219–227.

Welsby IJ, Monroe DM, Lawson JH, et al. Recombinant activated factor VII and the anaesthetist. *Anaesthesia.* 2005;60:1203–1212.

C.17. What laboratory tests should be ordered during the resuscitation of this patient?

Blood specimens for a hematocrit, hemoglobin level, platelet count, coagulation tests (aPTT, PT, and fibrinogen levels), and an arterial blood gas should be sent as soon as possible to determine an early baseline. During the resuscitation, the above blood tests should be sent periodically to help guide treatment including blood component therapy. If the volume of blood lost requires treatment with a massive transfusion, then electrolyte levels, including a potassium and calcium, also will need to be followed. Patients can develop hyperkalemia due to the elevated potassium levels in transfused blood and the cellular shifts caused by acidosis. Patients can develop hypocalcemia from citrate toxicity; citrate is the anticoagulant found in transfused pRBCs. Arterial blood gases and lactate levels also should be monitored to evaluate the acidosis that may develop due to poor tissue perfusion and the development of shock. If disseminated intravascular coagulation is a concern, the level of fibrin degradation product also should be checked.

Cunningham FG, Leveno KJ, Bloom SL, et al., eds. *Williams Obstetrics.* 23rd ed. New York: McGraw-Hill; 2010:787.

Townsend CM, Jr., Beauchamp RD, Evers BM, et al., eds. *Sabiston Textbook of Surgery.* 18th ed. Philadelphia: Saunders/Elsevier; 2008:86, 93–94.

C.18. Define amniotic fluid embolism (AFE) syndrome and discuss treatment.

AFE is a complex disorder that is poorly understood. Classically, it is characterized by the abrupt onset of a maternal collapse associated with hypotension, dyspnea, hypoxemia, cyanosis, loss of consciousness, seizures, cardiopulmonary arrest, and hemorrhaging associated with disseminated intravascular coagulation. There is, however, great individual variations in symptomatology from none to catastrophic systemic complications. The overall maternal mortality is reported to be between 22% and 90%. The reported incidence and outcome vary greatly in part because it is a diagnosis of exclusion and because of reporting bias with the syndrome being underdiagnosed in all but the most severe cases. The changing mortality rates may reflect improved intensive care and a recognition of the fact that "milder" cases do occur. Recently, Abenhaim et al. estimated an AFE incidence of 7.7 cases per 100,000 births in the United States. Advanced maternal age, placenta previa, and cesarean delivery

were risk factors, and maternal mortality was 21.6%. Clark et al. found a disappointingly high incidence of neurologic dysfunction among the surviving women that had a cardiac arrest as an initial symptom.

The cause of AFE syndrome is unknown. The detection of squamous cells, trophoblasts, and other debris of fetal origin is neither sensitive nor specific for AFE. Clark et al. suggested that the syndrome of acute peripartum hypoxia, hemodynamic collapse, and coagulopathy would be more aptly described as anaphylactoid syndrome of pregnancy than AFE. The suggestion that AFE may be related in some way to anaphylaxis has led to a number of reports describing tryptase levels in cases of AFE; however, some reported cases had elevated tryptase levels while others did not. A nine-case series suggests that complement activation, due to the low levels of complement found, rather than mast cell degranulation (anaphylaxis) plays a role in AFE. The diagnosis of AFE is a clinical one of exclusion; no diagnostic test exists. Treatment is prompt supportive resuscitation. There is no data that any type of intervention improves maternal prognosis with AFE although case reports using early hemofiltration or exchange transfusion exist.

Abenhaim HA, Azoulay L, Kramer MS, et al. Incidence and risk factors of amniotic fluid embolisms: a population-based study on 3 million births in the United States. *Am J Obstet Gynecol.* 2008;199(1):49.e1–e8.

Benson MD, Kobayashi H, Silver RK, et al. Immunologic studies in presumed amniotic fluid embolism. *Obstet Gynecol.* 2001;97:510–514.

Clark SL, Hankins GD, Dudley DA, et al. Amniotic fluid embolism: Analysis of the national registry. *Am J Obstet Gynecol.* 1995;172:1158–1169.

Cunningham FG, Leveno KJ, Bloom SL, et al., eds. *Williams Obstetrics.* 23rd ed. New York: McGraw-Hill, 2010:788–790.

Tufnell DJ. Amniotic fluid embolism. *Curr Opin Obstet Gynecol.* 2003;15(2):119–122.

D. Postoperative Management

D.1. If the patient received epidural anesthesia and subsequently developed disseminated intravascular coagulation (DIC), when should the epidural catheter be removed?

There is little information available concerning this topic. Sprung et al. made recommendations about the removal of an epidural catheter after DIC. First, they suggest that the patient's neurologic status be evaluated frequently and that the coagulopathy be treated; if there is no indication of intraspinal bleeding, they recommend removing the catheter as early as possible. If, however, bleeding is occurring around the catheter insertion site, the catheter may be left in place to tamponade this bleeding. Any neurologic deficits should be evaluated immediately; prompt surgical decompression may be needed. However, if a patient's neurologic status cannot be evaluated (e.g., postoperative intubation and sedation), an argument can be made for the removal of an indwelling catheter as soon as possible after the replacement of coagulation factors has created a state of normal coagulation even if it is temporary.

Chestnut DH, Polley LS, Tsen LC, et al., eds. *Chestnut's Obstetric Anesthesia: Principles and Practice.* 4th ed. Philadelphia: Mosby/Elsevier; 2009:847.

Sprung J, Cheng EY, Patel S. When to remove an epidural catheter in a parturient with disseminated intravascular coagulation? *Reg Anesth.* 1992;17(6):351–354.

D.2. You have successfully treated the patient's massive hemorrhage. Her laboratory values have returned to normal. Her central venous pressure (CVP) is within normal limits and urine output is appropriate. The patient, however, is still hypotensive despite appropriate intravascular volume replacement and support with vasopressors. What is your concern in this case?

She may have developed Sheehan syndrome. Sheehan syndrome refers to the development of a postpartum pituitary infarction with necrosis that is typically precipitated by an obstetric hemorrhage with severe hypotension. Sheehan syndrome is a rare complication. The damage to the pituitary may affect the secretion of one, several, or all of its hormones. Any of the manifestations of hypopituitarism (e.g., failure to lactate, amenorrhea/oligomenorrhea, hypotension, hyponatremia, hypothyroidism) can occur at any time from the immediate postpartum period to years after delivery. If the patient remains hypotensive after control of hemorrhage and adequate volume replacement, she should be evaluated and treated for adrenal insufficiency immediately; treatment of possible adrenal crisis should not be delayed while diagnostic tests are performed. Glucocorticoids have a role in maintaining peripheral vascular adrenergic tone, and the sudden loss of corticotropin (adrenocorticotropic hormone) secretion, particularly in conjunction with other serious physical stress, can lead to hypotension and shock. Prompt treatment with stress doses of glucocorticoids, (e.g., 4 mg dexamethasone by intravenous bolus) is necessary for survival. The work-up includes measuring adrenocorticotropic hormone, cortisol, thyroxine, prolactin, and growth hormone levels. The evaluation of other hormonal deficiencies is not urgent and can be deferred until 4 to 6 weeks postpartum.

Gabbe SG, Niebyl JR, Simpson JL, eds. *Obstetrics–Normal and Problem Pregnancies*. 5th ed. Philadelphia: Churchill Livingstone/Elsevier; 2007:78, 1039.

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CHAPTER 28

Hypertensive Disorders of Pregnancy

Sharon Abramovitz

A 39-YEAR-OLD WOMAN

gravida 1 para 0 at 29 weeks' gestation was admitted to the hospital because of an elevated blood pressure (BP) (182/111 mm Hg), headache, and proteinuria (6 g over a 24-hour period).

A. Medical Disease and Differential Diagnosis

1. What is the classification of hypertensive disorders in pregnancy as defined by the American College of Obstetricians and Gynecologists?
2. What is preeclampsia?
3. What is severe preeclampsia?
4. What is eclampsia?
5. What are the risk factors for developing preeclampsia?
6. What is the mortality associated with preeclampsia?
7. Discuss the pathogenesis of preeclampsia.
8. Discuss the pathologic alterations of preeclampsia.
9. Which component of BP best predicts the occurrence of preeclampsia?
10. What is the significance of increased pulse wave velocity (PWV) during pregnancy? How does this relate to birth weight?
11. What are some of the complications associated with preeclampsia?

B. Preoperative Evaluation and Preparation

1. What initial laboratory studies are recommended for patients with preeclampsia?
2. What are the important routine monitors for patients with preeclampsia? When is a central venous pressure monitor indicated?
3. What conditions mandate immediate delivery, regardless of the gestational age?
4. Discuss the obstetric management of preeclampsia.
5. In the United States, what drug therapy is the treatment of choice for seizure prophylaxis?

6. Discuss the treatment of magnesium sulfate toxicity.
7. Discuss the mechanism of action of magnesium sulfate.
8. What are the fetal effects of magnesium sulfate therapy?
9. Discuss the treatment of eclampsia.

C. Intraoperative Management

1. What is your choice of analgesia/anesthesia for patients with preeclampsia?
2. What is the advantage of prehydration?
3. How should patients be hydrated before epidural analgesia/anesthesia for labor and delivery?
4. Discuss bleeding time and platelet count evaluation during preoperative assessment of a patient with preeclampsia requesting epidural analgesia/anesthesia for labor and delivery.
5. What level of analgesia/anesthesia is required for labor and delivery?
6. Discuss the commonly used local anesthetics for labor analgesia.
7. Is the addition of epinephrine to local anesthetics advisable in preeclamptic patients?
8. What is the treatment for the abnormal fetal heart rate pattern seen with maternal hypotension after epidural analgesia/anesthesia is instituted?
9. What would you do after an accidental spinal tap? How do you treat postdural puncture headache?
10. How would you manage total spinal anesthesia?
11. Should ergonovine be given to preeclamptic patients?
12. When and how would you give spinal anesthesia?
13. Discuss a general anesthesia technique for the patient with preeclampsia presenting for cesarean delivery.
14. What agents can be used to prevent hypertension during the induction of general anesthesia for cesarean delivery?
15. What is HELLP syndrome?

D. Postoperative Management

1. Discuss the postpartum management of preeclamptic patients.

A. Medical Disease and Differential Diagnosis

A.1. What is the classification of hypertension disorders in pregnancy as defined by the American College of Obstetricians and Gynecologists?

Hypertensive disorders of pregnancy are classified as follows:

- Gestational hypertension
- Preeclampsia
  - Mild
  - Severe
- HELLP (hemolysis, elevated liver enzymes, low platelets) syndrome
- Chronic hypertension preceding pregnancy
- Chronic hypertension with superimposed preeclampsia

American College of Obstetricians and Gynecologists. *Hypertension in Pregnancy, ACOG Practice Bulletin, No. 33.* Washington, DC: American College of Obstetricians and Gynecologists; January 2002.

A.2. What is preeclampsia?

Preeclampsia is a multiorgan disease characterized by the development of hypertension with proteinuria after the 20th week of gestation. It is a disorder of unknown etiology affecting approximately 8% of all pregnancies, with most cases occurring during the first pregnancy. Hypertension is defined as a sustained systolic BP of at least 140 mm Hg or a diastolic BP of at least 90 mm Hg. Proteinuria is defined as 300 mg or more of protein in a 24-hour urine collection. Edema may manifest as a recent, rapid weight gain.

American College of Obstetricians and Gynecologists. *Hypertension in Pregnancy, ACOG Practice Bulletin, No. 33*. Washington, DC: American College of Obstetricians and Gynecologists; January 2002.

Sibai BM, Stella CL. Diagnosis and management of atypical preeclampsia-eclampsia. *Am J Obstet Gynecol*. 2009;200(5):481.e1–7.

A.3. What is severe preeclampsia?

Severe preeclampsia includes at least one of the following features:

- Blood pressure: systolic BP 160 mm Hg or higher or diastolic BP 110 mm Hg or higher on two occasions at least 6 hours apart; diagnosis not delayed if the diastolic BP exceeds 110 mm Hg
- Proteinuria: 5 g of protein or more in a 24-hour urine specimen (or 3 + to 4 + on semiquantitative urinalysis)
- Oliguria: urine output less than 500 mL in 24 hours
- Cerebral or visual disturbances: headache, blurred vision, or altered consciousness
- Pulmonary edema or cyanosis
- Epigastric or right upper quadrant pain, which may be caused by stretching of Glisson capsule by hepatic edema
- Hepatic rupture: rare complication
- Impaired liver function
- Thrombocytopenia: resulting from platelet adhesion to exposed collagen at sites of endothelial damage
- HELLP syndrome
- Evidence of fetal compromise (e.g., intrauterine growth retardation, oligohydramnios) or placental abruption

Chestnut DH, ed. *Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Elsevier Mosby; 2009:984.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone; 2008:561–566.

A.4. What is eclampsia?

Eclampsia is defined as convulsions and/or coma not caused by coincidental neurologic disease (e.g., epilepsy), which occurs during pregnancy or the puerperium in a woman whose condition also meets the criteria for preeclampsia.

Broughton-Pipkin F. The hypertensive disorders of pregnancy. *Br Med J*. 1995;311:609–613.

Chestnut DH, ed. *Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Elsevier Mosby; 2009:998–999.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone; 2008:561–566.

A.5. What are the risk factors for developing preeclampsia?

The risk factors for developing preeclampsia are as follows:

Hypertensive disease

- Previous preeclampsia
- Systolic hypertension during early pregnancy
- History of chronic hypertension
- Family history of hypertension during pregnancy
- Increase in pulse pressure during the first trimester

Coexisting vascular and endothelial disease

- Chronic renal disease
- Lupus erythematosus
- Protein S deficiency
- Activated protein C resistance
- Circulating anticardiolipin antibodies

Obstetric factors

- African American race
- Angiotensinogen gene *T235*
- Nulliparity
- Age older than 40 years
- History of smoking
- Obesity
- Increased trophoblastic mass (e.g., multiple gestation, molar pregnancy)
- Large for gestational age fetus
- Diabetes
- Erythroblastosis fetalis
- Polyhydramnios, particularly in young primigravidas

Boxer LM, Malinow AM. Preeclampsia and eclampsia. *Curr Opin Anesth*. 1997;10:188–198.

Chestnut DH, ed. *Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Elsevier Mosby; 2009:976–982.

A.6. What is the mortality associated with preeclampsia?

Hypertensive disorders of pregnancy account for 15% to 19% of maternal deaths in the United States and the United Kingdom.

American College of Obstetricians and Gynecologists. *Hypertension in Pregnancy, ACOG Practice Bulletin, No. 33*. Washington, DC: American College of Obstetricians and Gynecologists; January 2002.

Berg CJ, Atrash HK, Koonin LM, et al. Pregnancy-related mortality in the United States, 1987–1990. *Obstet Gynecol*. 1996;88:161–167.

Hibbard BM, Anderson MM, O'Driffe JO, et al. *Report on Confidential Enquiries into Maternal Deaths in the United Kingdom, 1991–1993*. London: HMSO; 1996:1–31.

A.7. Discuss the pathogenesis of preeclampsia.

Preeclampsia is most likely a disease of heterogeneous causes of both maternal and placental origin.

Immunologic factors

Immunologic disorders may arise from an abnormal maternal–fetal antigen–antibody response or from the contents of seminal fluids; spermatozoa may cause antibody formation or prostaglandins may initiate uterine vasoconstriction. The fetus acquires 50% of its genes from the father, which represents in part a paternal allograft that interacts with maternal tissue as the fetal trophoblast migrates into the maternal decidua after implantation. Migration normally occurs in two phases. Trophoblasts displace the muscular structure of the maternal spiral arteries before 20 weeks of gestation, causing their adrenergic denervation and converting them from high-resistance to low-resistance vessels. At the same time, biochemical adaptations occur in the maternal vasculature, with an increased dominance of endothelium-dependent vasodilators, prostacyclin (prostaglandin I [PGI]), and nitric oxide (NO). In preeclampsia, the second wave of trophoblastic migration fails. This failure can result in a high-resistance, low-flow uteroplacental circulation and consequent placental ischemia and hypoxia. These changes may represent an aberrant immunologic mechanism.

Genetic factors

A familial tendency toward preeclampsia exists in some populations, and it may result from a recessive genetic inheritance.

Endothelial factors

Vascular endothelial damage or dysfunction is the common pathologic feature of preeclampsia and occurs in the placental decidual vessels and renal microvasculature. Endothelial cell dysfunction in response to unknown factors may cause a hormonal imbalance in women with preeclampsia (Fig. 28.1).

The metabolic end products of normal vascular endothelium include PGI_2 and endothelium-derived relaxing factor (EDRF), which is either NO or a related nitrosyl substance. Both PGI_2 and EDRF are potent vasodilators. In patients with preeclampsia, the failure of the trophoblast to invade the uteroplacental vascular bed may encourage an increased production of free radicals and lipid peroxides by the decidual lymphoid tissue. As a result, an imbalance occurs between the production of the vasoconstrictor thromboxane A_2 (TXA_2), which is derived from platelets, and the production of endothelium-derived PGI_2. This imbalance results in a reduced perfusion of the intervillous space. Some investigators have concluded that hypoxia-induced impairment of NO production by the syncytiotrophoblast results in uteroplacental insufficiency and production of a toxin responsible for the clinical manifestations of preeclampsia.

It has been shown that production of endothelin 1 (ET-1), which is the most potent endogenous vasoconstrictor and produced mainly by vascular smooth muscle cells as well as by the vascular endothelium, is markedly increased in preeclampsia and correlates inversely with NO production. Therefore, the imbalance between NO and ET-1 may play a significant role in the pathophysiology of preeclampsia.

Fetoplacental blood vessels, namely, the human placental chorionic plate arteries, constrict in response to ET-1. Moreover, there is now some evidence that amniotic concentration of ET-1 is elevated in pregnancies associated with preeclampsia. Margarit et al. found a statistically significant increase in ET-1 concentration in the aminionic fluid of women at 17 weeks' gestation who developed preeclampsia, as compared to those who did not develop preeclampsia. By the second trimester, higher levels of ET-1 have also been shown in the amniotic fluid of women with preterm premature rupture of the membranes.

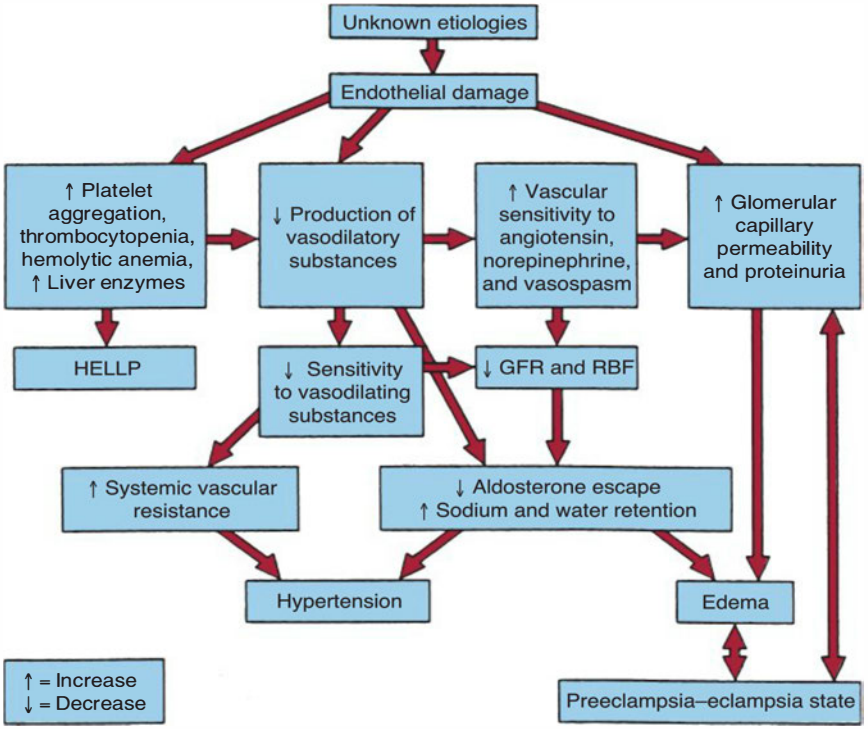

Figure 28.1 Endothelial cell dysfunction in response to unknown factors may cause a hormonal imbalance in women with pregnancy-induced hypertension. GFR, glomerular filtration rate; HELLP, hemolysis, elevated liver enzymes, low platelets; RBF, renal blood flow. (From Chestnut DH, ed. *Obstetric Anesthesia: Principles and Practice.* 3rd ed. Philadelphia: Mosby; 2004:798, with permission.)

Platelet factors

In mild preeclampsia, serotonin (5-HT) released from aggregating platelets interacts with endothelial 5-HT_1 receptors, resulting in the release of prostacyclin and NO (EDRF). The released prostacyclin induces angiotensin II release, improving uteroplacental perfusion. In early-onset severe preeclampsia, damaged uteroplacental vessels cannot respond to 5-HT_1 effects. Instead, serotonin interacts with 5-HT_2 receptors on vascular smooth muscle cells, inducing vasoconstriction. Platelet-derived serotonin also activates 5-HT_2 platelet receptors, establishing a positive feedback loop and intensifying platelet aggregation. The loss of 5-HT_1 receptors prevents stimulation of angiotensin II release (Fig. 28.2).

Calcium

In normal pregnancy, the intracellular free calcium concentration increases slowly, but this increase is significantly greater in the third trimester in women with preeclampsia. The increase in cytoplasmic calcium levels is enhanced by angiotensin II, and the enhancement is greater in women with preeclampsia compared with normotensive women. This response to angiotensin II occurs long before signs of preeclampsia become evident and is a sensitive indicator of its subsequent development.

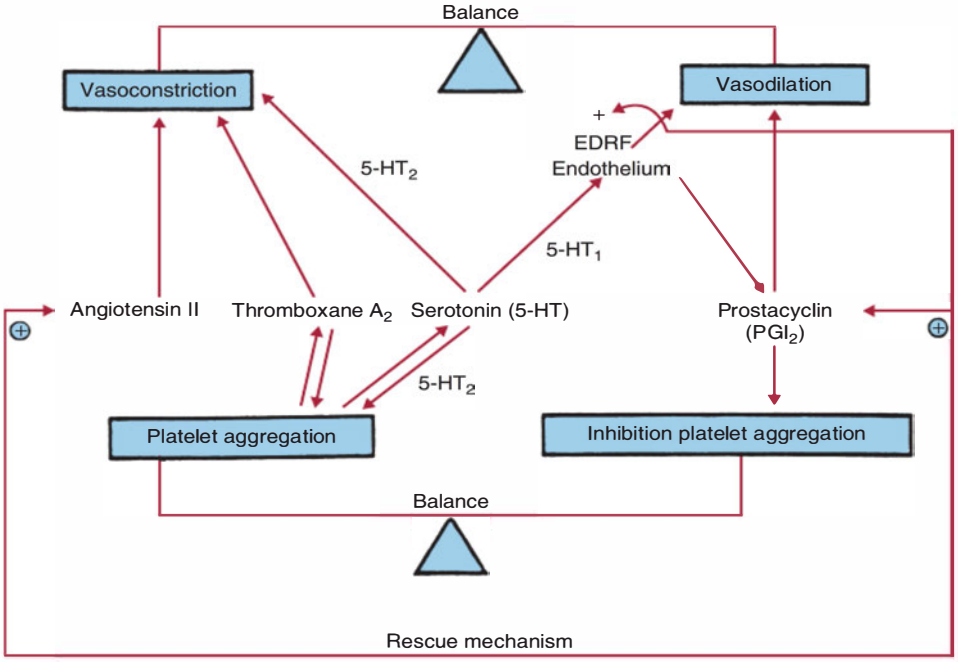

Figure 28.2 The loss of 5-HT_1 receptors prevents stimulation of angiotensin II release. EDRF, endothelium-derived relaxing factor. (From Chestnut DH, ed. *Obstetric Anesthesia: Principles and Practice.* 3rd ed. Philadelphia: Mosby; 2004:797, with permission.)

Coagulation factors

Platelet activation in preeclampsia is surface mediated. Women with preeclampsia have an increased tendency toward thromboembolism, which may result in part from an alteration in the plasma ratio between von Willebrand factor and factor VIII coagulant activity.

Fatty acid metabolism

Altered handling of fatty acids by the liver is a key factor in the pathogenesis of preeclampsia. Both increased hepatic uptake of free fatty acids and hypertriglyceridemia are seen more frequently in women who develop preeclampsia.

Markers of angiogenesis

Preeclamptic patients have elevated plasma levels of endoglin and soluble FLT-1, the receptor for vascular endothelial growth factor, throughout gestation. Recent research suggests that these molecules are not just disease markers but are involved in the pathogenesis of preeclampsia.

Baksu B, Davas I, Baksu A, et al. Plasma nitric oxide, endothelin -1 and urinary nitric oxide and cyclic guanosine monophosphate levels in hypertensive pregnant women. *Int J Gynaecol Obstet.* 2005;90(2):112–117.

Broughton-Pipkin F, Rubin PC. Preeclampsia: the "disease of theories." *Br Med Bull.* 1994;50:381–396.

Chestnut DH, ed. *Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Elsevier Mosby; 2009:975–1007.

DeJong CL, Dekker GA, Sibai BM. The renin-angiotensin-aldosterone system in pre-eclampsia: a review. *Clin Perinatol*. 1991;18:683–711.

Dekker GA, Sibai BM. Etiology and pathogenesis of preeclampsia: current concepts. *Am J Obstet Gynecol*. 1998;179:1359–1375.

Lindoff C, Ingemarsson I, Martinsson G, et al. Preeclampsia is associated with a reduced response to activated protein C. *Am J Obstet Gynecol*. 1997;176:457–460.

Margarit L, Griffiths A, Tsapanos V, et al. Second trimester amniotic fluid endothelin concentration. A possible predictor for pre-eclampsia. *J Obstet Gynaecol*. 2005; 25(1):18–20.

Venkatesha S, Toporsian M, Lam C, et al. Soluble endoglin contributes to the pathogenesis of preeclampsia. *Nat Med*. 2006;12:642–649.

Zeeman GG, Dekker GA. Pathogenesis of preeclampsia: a hypothesis. *Clin Obstet Gynecol*. 1992;35:317–337.

Zuspan FP. New concepts in the understanding of hypertensive diseases during pregnancy: an overview. *Clin Perinatol*. 1991;18:653–659.

A.8. Discuss the pathologic alterations of preeclampsia.

Cardiovascular changes

- *Blood pressure*. Increase in BP results from an increase in peripheral vascular resistance secondary to a state of sympathetic overactivity. Alternatively, systolic BP increases as a result of increased cardiac output (increased plasma volume—typical of pregnancy) and a noncompliant aorta. In such cases, the systemic vascular resistance (SVR), which is predominantly determined by the smaller arterioles, is not increased but due to aortic stiffness, the ejected stroke volume causes the systolic component to rise significantly.
- *Blood volume*. Reduction in blood volume causes a greater degree of hemoconcentration.

Hemodynamic changes

- Three hemodynamic subsets exist:
  - *Hyperdynamic* with increased cardiac output, normal or slightly increased SVR, and normal or slightly decreased blood volume and filling pressures
  - *High SVR* with normal cardiac output and lower filling pressures
  - *Markedly increased SVR* with decreased blood volume and depressed left ventricular function
- Poor correlation between central venous pressure (CVP) and pulmonary artery (PA) occlusion pressure
- Decreased colloid oncotic pressure in pregnancy with further reduction in preeclampsia. The low colloid oncotic pressure, coupled with increased vascular permeability and the loss of intravascular fluid and protein into interstitial tissues, increases the risk of pulmonary edema.

Hematologic changes

- Hypercoagulable state (Table 28.1)
- Platelet activation: Thrombocytopenia occurs in 15% to 30% of women with preeclampsia or eclampsia. Preeclampsia may be associated with a significant defect in *both* platelet function and platelet number. Thrombocytopenia without other coagulation abnormalities but with evidence of hemolysis and increased liver enzymes characterizes HELLP syndrome.

Table 28.1 Changes that Imply Hypercoagulation in Preeclampsia

↑ Common pathway activity
↓ Fibrinogen
↑ Fibrin-degradation products
D-Dimer positive
↑ Fibrinopeptide A
↑ Factor VIII antigen; factor VIII activity
↓ Antithrombin-III
↑ Antithrombin-III/antithrombin complex
↓ Platelets
↑ β-Thromboglobulin
↑ Platelet aggregability
↓ Sensitivity to prostacyclin

From Chestnut DH. *Obstetric Anesthesia: Principles and Practice.* 3rd ed. Philadelphia: Mosby, 2004:803, with permission.

Renal changes

- Glomerular enlargement results in ischemia, leading to decreased glomerular filtration rate.
- Proteinuria occurs as a result of an increased permeability to most large molecular weight proteins.
- Urate clearance decreases and serum uric acid concentrations increase. Hyperuricemia may provide an early indication of preeclampsia.
- Oliguria parallels the severity of preeclampsia.

Endocrine changes

In women with preeclampsia, a breakdown of the normal balance between vasodilators (PGI_2, NO) and vasoconstrictors (angiotensin II, TXA_2, serotonin, endothelin) occurs. There is also a decrease in plasma renin concentration and a suppression of the renin–angiotensin–aldosterone system.

Respiratory changes

- Pharyngeal and laryngeal edema may make airway management difficult, necessitating the use of smaller endotracheal tubes.
- Pulmonary edema occurs in 3% of cases, with some cases occurring postpartum.

Hepatic changes

- Serum transaminase levels frequently increase in patients with mild preeclampsia.
- Epigastric or subcostal pain is an ominous symptom that is typically caused by distension of the liver capsule by edema or subcapsular or parenchymal bleeding. Hepatic swelling produces epigastric pain.
- Liver rupture is associated with more than 80% mortality.

Neurologic changes

- The classic manifestations of preeclampsia include severe headache, visual disturbances, central nervous system hyperexcitability, and hyperreflexia.

- The occurrence of seizures indicates eclampsia until proved otherwise. Etiologies of seizures include hypertonic encephalopathy, vasospasm, microinfarctions and punctate hemorrhages, thrombosis, and cerebral edema.
- Postpartum eclampsia may occur up to 10 days after delivery.

Uteroplacental perfusion

- Uteroplacental perfusion is decreased in preeclampsia with the potential for intrauterine growth retardation.

Benigni A, Orisio S, Gaspari F, et al. Evidence against a pathogenic role for endothelin in preeclampsia. *Br J Obstet Gynaecol*. 1992;99:798–802.

Chestnut DH, ed. *Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Elsevier Mosby; 2009:975–1007.

DeJong CL, Dekker GA, Sibai BM. The renin–angiotensin–aldosterone system in preeclampsia: a review. *Clin Perinatol*. 1991;18:683–711.

Inayatulla A, Chemtob S, Nuwayhid B, et al. Responses of placental arteries from normotensive and preeclamptic women to endogenous vasoactive agents. *Am J Obstet Gynecol*. 1993;168:869–874.

Perry KG, Martin JN. Abnormal hemostasis and coagulopathy in preeclampsia and eclampsia. *Clin Obstet Gynecol*. 1992;35:338–350.

Seligman SP, Buyon JP, Clancy RM, et al. The role of nitric oxide in the pathogenesis of preeclampsia. *Am J Obstet Gynecol*. 1994;171:944–948.

A.9. Which component of BP best predicts the occurrence of preeclampsia?

Pregnancy induces several cardiovascular responses and adaptation that include increases in vascular and extravascular volume, higher cardiac output, and marked reduction in peripheral resistance that effectively causes a relatively lower BP by the second trimester of pregnancy. Multiple attempts have been made to correlate first and second trimester systolic, diastolic, and mean arterial pressures (MAP) with development of preeclampsia. Unfortunately, there is significant variability in the aforementioned components of BP throughout pregnancy, complicated further by factors such as ethnicity, age, nulliparous versus multiparous state, and gestational differences at the time of measurements. In addition, the anxiety component of an office visit (white-coat effect) frequently contributes to variability in measures of BP, limiting their predicatibility of preeclampsia. Ravi et al. reported that although systolic, diastolic, and MAP were elevated in women who developed hypertensive disorder of pregnancy as compared to normotensive women, these parameters did not correlate with ensuing preeclampsia. Conversely, elevations in pulse pressure at 7 to 15 weeks of gestation was a significant predictor of preeclampsia but not of gestational hypertension. In fact, for every 1 mm Hg increase in pulse pressure, the associated risk of preeclampsia increased by 6%.

Ravi T, Ecker JL, Kettyle E, et al. Pulse pressure and risk of preeclampsia: a prospective study. *Obstet Gynecol*. 2001;97:515–520.

A.10. What is the significance of increased pulse wave velocity (PWV) during pregnancy? How does this relate to birth weight?

Similar to increase in pulse pressure, PWV can be a marker of arterial stiffness. In normal pregnancy, arterial stiffness decreases during the first trimester and remains low until the end of pregnancy due to either reduced smooth muscle tone or vessel

wall remodeling. However, there is a wide range in arterial stiffness even in normal pregnancy, suggesting a varying degree of cardiovascular adaptation. Maladaptation may lead to retardation in fetal growth as measured by birth weight and by postnatal catch-up growth. Elvan-Taspinar et al. found a significant relation between PWV during the last trimester of pregnancy and fetal birth weight and postnatal catch-up growth independent of MAP. For example, an increase in PWV of 1 m per second was associated with a decrease in birth weight by 17.6%. Similarly, a strong link was found between pulse pressure and birth weight, with an increase of 10 mm Hg in pulse pressure being associated with an 11.8% decrease in weight. Both PWV and pulse pressure appear to offer superior circulatory as well as prognostic information relating to fetal and neonatal outcome.

Elvan-Taspinar A, Franx A, Bots ML, et al. Arterial stiffness and fetal growth in normotensive pregnancy. *Am J Hematol*. 2005;18:337–341.

Lurbe E, Torro I, Alvarez V, et al. The impact of birth weight on pulse pressure during adolescence. *Blood Press Monit*. 2004;9:187–192.

Spasojevic M, Smith S, Morris J, et al. Peripheral arterial pulse wave analysis in women with preeclampsia and gestational hypertension. *Int J Gynaecol Obstet*. 2005;112:1475–1478.

A.11. What are some of the complications associated with preeclampsia?

Maternal complications include disseminated intravascular coagulation, congestive heart failure with pulmonary edema, placental abruption, postpartum hemorrhage, acute renal failure, rupture of the liver, cerebrovascular accident, and septic shock. The leading cause of maternal death is intracranial hemorrhage.

Fetal complications include prematurity with respiratory distress, intrauterine growth retardation, oligohydramnios, intracranial hemorrhage, small for gestational age, and aspiration of meconium. The leading cause of intrauterine morbidity and mortality is uteroplacental insufficiency caused by placental infarcts, followed by placental abruption, and chorioamnionitis.

Datta S, ed. *Anesthetic and Obstetric Management of High-risk Pregnancy*. 3rd ed. New York: Springer; 2004:270–281.

B. Preoperative Evaluation and Preparation

B.1. What initial laboratory studies are recommended for patients with preeclampsia?

- Complete blood cell count
- Platelet count and aggregation when available
- Coagulation assay including activated partial thromboplastin time, prothrombin time, fibrinogen, D-dimer
- Serum electrolytes
- Blood urea nitrogen, creatinine, and uric acid concentration
- Liver function tests
- Urinalysis, microscopy, 24-hour specimen for protein and creatinine clearance
- Type and screen (cross-match if antibodies present)

Chestnut DH, ed. *Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Elsevier Mosby; 2009:975–1007.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease.* 5th ed. Philadelphia: Churchill Livingstone; 2008:561–566.

B.2. What are the important routine monitors for patients with preeclampsia? When is a central venous pressure monitor indicated?

Important routine monitors are as follows:

- Noninvasive BP
- Maternal respiratory function assessment with oxygen saturation
- Hourly deep tendon reflexes
- Muscle strength
- Serial magnesium sulfate levels
- Foley catheter for assessing urine output
- Uterine contraction monitor
- Continuous fetal heart rate monitoring
- Consider invasive BP monitoring with an arterial line when severe refractory hypertension is present; when rapid-acting vasodilators, such as sodium nitroprusside (SNP) or nicardipine, are used; or when noninvasive BP measurement proves difficult (e.g., obesity).
- A CVP monitor or a PA catheter may be indicated for the following conditions:
  - Persistent oliguria
  - Difficulty in fluid management therapy in antepartum and/or postpartum period
  - Presence of pulmonary edema

A survey on the use of invasive hemodynamic monitoring among anesthesiologists who care for patients with preeclampsia indicates that central monitoring is used in 7.5% of patients. When invasive hemodynamic monitoring is used, 56% of anesthesiologists use an arterial line, 26% use an arterial line and central monitoring, and 20% use central monitoring only. Also, 92% of respondents use a CVP monitor, whereas only 8% use a PA catheter. The etiology of pulmonary edema, however, may be due to an increase in capillary permeability as well as from diastolic dysfunction, complicating assessment of cardiac function and volume status. Only in severe forms of preeclampsia is left ventricular systolic function markedly reduced. Further, there may be technical difficulties with placing the PA catheter that are both patient related (awake, anxious, short neck with poorly visible landmarks, coagulopathy) and physician related (inexperience with central venous catheterization), which may alter the balance between benefit and risk of invasive monitoring. Whenever possible, a bedside transthoracic echocardiogram may be obtained; however, there may be limited windows for imaging due to the gravid uterus—causing distention of the abdomen.

Birnbach DJ, Gatt SP, Datta S, eds. *Textbook of Obstetric Anesthesia*. 1st ed. New York: Churchill Livingstone; 2000:546.

Ross VH, Moore CH, Fragneto RY, et al. Invasive hemodynamic monitoring in the management of PIH: a survey of practicing anesthesiologists. *Anesthesiology.* 2000;92:A89.

B.3. What conditions mandate immediate delivery, regardless of the gestational age?

- Severe hypertension that persists after 24 to 48 hours
- Progressive thrombocytopenia
- Liver dysfunction

- Progressive renal dysfunction (including severe oliguria)
- Premonitory signs of eclampsia
- Evidence of fetal jeopardy
- Persistent headache or other neurologic sequelae of preeclampsia

Datta S, ed. *Anesthetic and Obstetric Management of High-risk Pregnancy.* 3rd ed. New York: Springer; 2004:407–408.

B.4. Discuss the obstetric management of preeclampsia.

The goal of therapy is to stabilize the mother and to safely deliver the fetus and placenta.

- Improve intravascular volume.
- Administer seizure prophylaxis with magnesium sulfate.
- Administer antihypertensives for BP control.

Labetalol is a commonly used antihypertensive agent that decreases maternal SVR without increasing maternal heart rate or decreasing cardiac index, uterine blood flow, or fetal heart rate when it is given in a total dose of less than 1 mg per kg. When given in an initial intravenous bolus dose of 10 to 20 mg, it has a faster onset of action than hydralazine and, if necessary, the dose may be doubled every 10 minutes. It is useful in the management of refractory hypertension. If a second agent must be administered (e.g., hydralazine, SNP, or nicardipine), labetalol helps to prevent reflex tachycardia. It is important to note that the mechanism of hypertension is mediated greatly by circulating catecholamines, making labetalol a preferred antihypertensive agent that will antagonize the vasoconstrictive effects of norepinephrine, in particular. Other agents may reduce the BP as reflected by a peripheral BP monitor; however, unopposed vasoconstriction at the central and at the microcirculatory levels may cause end-organ injury.

Hydralazine is another antihypertensive agent that can be used because of its direct vasodilating effect. The full extent of its effect is evident in 20 minutes; therefore, if sufficient time is not allowed between injections, severe hypotension will be seen. It is used in 5- to 10-mg increments intravenously every 20 to 30 minutes until the diastolic BP is decreased, with a cumulative dose of 20 mg. Hydralazine directly decreases peripheral vascular resistance. Reflex sympathetic activity can result in tachycardia and increased stroke volume and cardiac output. Tachycardia can be treated with labetalol, 10 to 20 mg intravenously. The patient may complain of headache and flushing of the face during therapy.

Nitroglycerin (NTG) causes vascular smooth muscle relaxation by means of its intracellular degradation to NO. The primary effect of NTG is venodilation, but it is less effective in prehydrated patients. NTG readily crosses the placenta. The drug is most useful for short-term treatment (e.g., to control the pressor response to tracheal intubation). Small doses, 50 to 100 μg, may be given intravenously, or NTG may be given sublingually in a 400-μg metered spray.

SNP relaxes the arterial vessels, thereby reducing afterload. However, SNP also reduces venous return. The drug is most useful for short-term treatment, similar to NTG. Cyanide toxicity is proposed to be more likely with prolonged infusion rates that exceed 4 μg/kg/minute over several hours to days; however, Naulty et al. demonstrated that intravenous infusion of nitroprusside solution in pregnant ewes, maintained at a rate sufficient to decrease mean maternal arterial pressure by 20% for 1 hour, resulted in equilibration of maternal and fetal levels of nitroprusside at the 20-minute sample. Five of the eight animals exhibited tachyphylaxis

to nitroprusside, and their fetuses died in utero with lethal levels of cyanide. No significant changes were observed in uterine blood flow. There have been attempts to counteract the cyanide toxicity of nitroprusside by coadministration of sodium thiosulfate. Curry et al. administered sodium thiosulfate and nitroprusside to pregnant ewes and only nitroprusside to a control group. Although control ewes and fetuses suffered progressive increases in red cell cyanide concentrations into the toxic range, experimental ewes and fetuses never developed toxic red cell cyanide levels. These results suggest that coadministration of sodium thiosulfate with SNP to pregnant women at doses currently in use for nonpregnant patients will prevent fetal, as well as maternal, cyanide toxicity. Unfortunately, it is not known whether these findings are transferable to humans, raising major concern over ongoing clinical use of nitroprusside in obstetrics when safer drugs such as nicardipine and labetalol are available.

Nifedipine is a calcium entry blocker that affects predominantly arterial and arteriolar smooth muscle. Common maternal side effects include facial flushing, headache, and tachycardia. Nifedipine rapidly lowers BP after oral or sublingual administration. After an initial dose of 10 mg sublingually, it may be repeated in 30 minutes and subsequently given in a maintenance dose of 10 to 20 mg every 3 to 6 hours. Caution must be exercised in the patient receiving both magnesium sulfate and calcium entry blockers because of the risk of myocardial depression and resultant pulmonary edema.

Chestnut DH, ed. *Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Elsevier Mosby; 2009:975–1007.

Curry SC, Carlton MW, Raschke RA. Prevention of fetal and maternal cyanide toxicity from nitroprusside with coinfusion of sodium thiosulfate in gravid ewes. *Anesth Analg*. 1997;84(5):1121–1126.

Lopez-Jaramillo P, Narvaez M, Calle A, et al. Cyclic guanosine 3′5′ monophosphate concentrations in preeclampsia: effects of hydralazine. *Br J Obstet Gynaecol*. 1996;103:33–38.

Naulty J, Cefalo RC, Lewis PE. Fetal toxicity of nitroprusside in the pregnant ewe. *Am J Obstet Gynecol*. 1981;139(6):708–711.

B.5. In the United States, what drug therapy is the treatment of choice for seizure prophylaxis?

Magnesium sulfate is the initial therapy for seizure prophylaxis. The Eclampsia Trial Collaborative Group compared magnesium sulfate, phenytoin, and diazepam administration for the prevention of recurrent seizures in women with preeclampsia. They found that magnesium sulfate was more effective in preventing recurring seizures than either phenytoin or diazepam.

An initial bolus of 4 to 6 g of magnesium sulfate is administered over 20 minutes and followed with an intravenous infusion of 1 to 2 g per hour. Urine output, respiratory rate, and patellar reflexes are monitored during magnesium therapy. The serum magnesium sulfate concentration should be measured at least 4 hours after initiation of therapy. The therapeutic range for serum magnesium sulfate concentrations is between 4 and 6 mEq per L. Loss of deep tendon reflexes occurs at 10 mEq per L with evidence of prolonged P-Q intervals and widening QRS complexes. Respiratory arrest occurs at 15 mEq per L, and asystole occurs at 20 mEq per L.

Eclampsia Trial Collaborative Group. Which anticonvulsant for women with eclampsia? Evidence from the collaborative eclampsia trial. *Lancet*. 1995;345:1455–1463.

B.6. Discuss the treatment of magnesium sulfate toxicity.

Magnesium sulfate is excreted by the kidneys. Therefore, urine output must be followed closely and serial serum concentrations of magnesium sulfate must be checked, especially in women with renal dysfunction. If magnesium sulfate toxicity is suspected, the magnesium sulfate infusion should be immediately discontinued. Intravenous calcium gluconate, 1 g, or calcium chloride, 300 mg, should be administered if needed to antagonize the effects of magnesium sulfate. If respiratory distress occurs, the patient may require endotracheal intubation and mechanical ventilation.

Chestnut DH, ed. *Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Elsevier Mosby; 2009:975–1007.

B.7. Discuss the mechanism of action of magnesium sulfate.

Magnesium has the following effects:

- It is a central nervous system depressant and anticonvulsant.
- It inhibits the release of acetylcholine at the neuromuscular junction, decreases the sensitivity of the motor end plate to acetylcholine, and decreases muscle membrane excitability, thereby potentiating the effects of nondepolarizing and depolarizing muscle relaxants.
- It decreases uterine hyperactivity by its mild relaxant effect on vascular and uterine smooth muscle; it may improve uterine blood flow.
- It is a mild vasodilator in vascular beds (including small-diameter cerebral vessels) by a direct or indirect (calcium-competing) effect; and it has a mild antihypertensive effect.

Chestnut DH, ed. *Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Elsevier Mosby; 2009:975–1007.

B.8. What are the fetal effects of magnesium sulfate therapy?

Magnesium sulfate crosses the placenta. There can be evidence of decreased beat-to-beat variability in the fetal heart rate. Neonatal depression (e.g., respiratory depression and hyporeflexia) also can occur.

Chestnut DH, ed. *Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Elsevier Mosby; 2009:975–1007.

B.9. Discuss the treatment of eclampsia.

- Stop the convulsions (e.g., thiopental, 50 to 100 mg intravenously).
- Establish an airway.
- Turn patient to the left side; apply jaw thrust.
- Attempt bag and mask ventilation.
- Insert oropharyngeal airway if necessary.
- Maintain ventilation and oxygenation.
- Continue bag and mask ventilation.
- Apply pulse oximeter and monitor.
- Maintain circulation.

- Secure intravenous access.
- Check BP at frequent intervals.
- Monitor electrocardiographic (ECG) recordings.
- Administer magnesium sulfate.
- Treat hypertension.
- Deliver the baby expeditiously.

Chestnut DH, ed. *Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Elsevier Mosby; 2009:999.

C. Intraoperative Management

C.1. What is your choice of analgesia/anesthesia for patients with preeclampsia?

Most anesthesiologists and obstetricians consider epidural analgesia the preferred form of pain relief for labor and delivery in preeclamptic women. Epidural analgesia provides the following advantages:

- Epidural analgesia provides pain relief that is superior to all other analgesic methods.
- Epidural analgesia attenuates the exaggerated hypertensive response to pain of preeclamptic women.
- Epidural analgesia reduces circulating levels of catecholamines and stress-related hormones, which facilitates BP control.
- Epidural analgesia may improve intervillous blood flow in preeclamptic women.
- Epidural analgesia results in stable cardiac output.
- Preeclamptic women are at increased risk of cesarean delivery compared with normal parturients, and early administration of epidural analgesia for labor facilitates the subsequent administration of epidural anesthesia for emergent cesarean delivery.

Benedetto C, Zonca M, Marozio L, et al. Blood pressure patterns in normal pregnancy and in pregnancy-induced hypertension, preeclampsia, and chronic hypertension. *Obstet Gynecol*. 1996;88:503–510.

Chestnut DH, ed. *Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Elsevier Mosby; 2009:975–1007.

Cunningham FG, Lindheimer MD. Hypertension in pregnancy. *N Engl J Med*. 1992;326:927–932.

C.2. What is the advantage of prehydration?

Prehydration helps compensate for reductions in preload and afterload during the administration of epidural analgesia/anesthesia. Two studies have investigated the effects of intravenous volume loading with crystalloid on atrial natriuretic peptide (ANP) secretion in preeclamptic women. ANP is a vasodilator secreted from the cardiac atria in response to an acute volume load, and this response is more pronounced in preeclamptic women. ANP has properties that counteract vasospasm and improve renal elimination of excess extracellular fluid. These studies support the use of volume expansion before administration of regional anesthesia in preeclamptic women.

However, in current practice, lower concentrations of local anesthetics combined with an opioid are used for labor analgesia, and fluid preloading is of less clinical relevance. One still needs to be vigilant to the risk of pulmonary edema in the severely preeclamptic patient.

Chestnut DH, ed. *Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Elsevier Mosby; 2009:992–993.

C.3. How should patients be hydrated before epidural analgesia/anesthesia for labor and delivery?

Most preeclamptic patients may receive prehydration with crystalloid in a 10 mL per kg bolus. Attention must be given to evidence of recent excessive weight gain or a fluid balance chart suggesting overhydration. Also, one must monitor for the development of pulmonary edema. Additional crystalloid (e.g., 250 to 500 mL) can be infused if hypotension ensues during epidural analgesia/anesthesia.

Datta S, ed. *Anesthetic and Obstetric Management of High-risk Pregnancy*. 3rd ed. New York: Springer; 2004:285–286.

C.4. Discuss bleeding time and platelet count evaluation during preoperative assessment of a patient with preeclampsia requesting epidural analgesia/anesthesia for labor and delivery.

The bleeding time does not specifically measure platelet function, and it can be abnormal in a number of coagulation disorders, such as factor deficiencies. No evidence suggests that the skin bleeding time predicts the potential for bleeding from a traumatized epidural vein in a woman with severe preeclampsia. Therefore, the bleeding time should not be used to measure platelet function. A specific platelet count that predicts the risk of complications from regional anesthesia has not been determined. The *trend* in platelet count is important to note, as preeclampsia is a dynamic disorder, and a rapid decrease in platelet count in a short interval may warrant concern.

Many anesthesiologists will place an epidural anesthetic at a platelet count of 80,000 per μL and some at lower platelet counts. The patient must be individualized and a thorough bleeding history, along with the trend in platelet count, should be considered.

Beilin Y, Zahn J, Comerford M. Safe epidural analgesia in thirty parturients with platelet counts between 69,000 and 98,000 mm(−3). *Anesth Analg*. 1997;85:385–388.

Chestnut DH, ed. *Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Elsevier Mosby; 2009:992.

C.5. What level of analgesia/anesthesia is required for labor and delivery?

- First stage of labor: T10-L1
- Second stage of labor: S2–4

Chestnut DH, ed. *Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Elsevier Mosby; 2009:387–392.

C.6. Discuss the commonly used local anesthetics for labor analgesia.

Bupivacaine, ropivacaine, and levobupivacaine (amide local anesthetics) are commonly used because they provide potent analgesia. They provide analgesia with less motor block than an equipotent concentration of lidocaine. Moreover, dilute solutions cause less hypotension than more concentrated solutions.

Bupivacaine is four times more potent than lidocaine. It is 90% to 95% bound to maternal plasma protein. It is known to be more cardiotoxic than lidocaine. The mechanism relates to its action on cardiac sodium channels. Bupivacaine and lidocaine both block sodium channels to the nerves and to the heart. They are similar because they both cause a rapid block of cardiac sodium channels on depolarization. They differ in their recovery from block. The lidocaine block is complete within less than 1 second, whereas bupivacaine takes five times longer. Bupivacaine is a "fast-in, slow-out" agent. Its main advantage is that it has a longer duration and a weak motor block when given in analgesic concentrations.

Ropivacaine is a homolog of mepivacaine and bupivacaine, but it is formulated as a single levorotatory isomer rather than as a racemic mixture. It appears to be less cardiotoxic than bupivacaine.

Levobupivacaine is also a single levorotatory isomer formulation of a local anesthetic. Levobupivacaine appears to be less cardiotoxic than bupivacaine.

2-Chloroprocaine is an ester type of local anesthetic. It is hydrolyzed by plasma cholinesterase, and it has a rapid metabolism, allowing for a very quick onset of action.

Chestnut DH, ed. *Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Elsevier Mosby; 2009:247–252.

Mazoit JX, Boico O, Samii K. Myocardial uptake of bupivacaine, II: pharmacokinetics and pharmacodynamics of bupivacaine enantiomers in the isolated perfused rabbit heart. *Anesth Analg*. 1993;77:477–482.

Valenzuela C, Snyders DJ, Bennett PB, et al. Stereoselective block of cardiac sodium channels by bupivacaine in guinea pig ventricular myocytes. *Circulation*. 1995; 92:3014–3024.

C.7. Is the addition of epinephrine to local anesthetics advisable in preeclamptic patients?

Clinical evidence supports the safety of epidural administration of an epinephrine-containing local anesthetic in preeclamptic women. However, care must be taken when using epinephrine-containing local anesthetic solutions in severe preeclamptic women as inadvertent intravascular injection may result in acute severe hypertension.

Chestnut DH, ed. *Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Elsevier Mosby; 2009:993.

Dror A, Abboud TK, Moore J, et al. Maternal hemodynamic responses to epinephrine-containing local anesthetics in mild preeclampsia. *Reg Anesth*. 1988;13:107–111.

Heller PJ, Goodman C. Use of local anesthetics with epinephrine for epidural anesthesia in preeclampsia. *Anesthesiology*. 1986;65:224–226.

C.8. What is the treatment for the abnormal fetal heart rate pattern seen with maternal hypotension after epidural analgesia/anesthesia is instituted?

- Administration of oxygen with face mask
- Left uterine displacement
- Increased hydration

- Elevation of lower extremities to facilitate venous return
- Administration of small increments of ephedrine, 2.5 to 5 mg or phenylephrine, 50 to 100 μg intravenously, if the BP falls more than 20% of baseline.

Vercateren M. Obstetric spinal analgesia and anesthesia. *Curr Opin Anesthesiol.* 2003;16:503–507.

C.9. What would you do after an accidental spinal tap? How do you treat postdural puncture headache?

Accidental dural puncture can be managed with one of two options. First, the epidural needle may be repositioned in another interspace. Local anesthetic must be administered slowly because now there is a direct communication with the intrathecal space through the dural hole, and thereby, a more profound analgesic/anesthetic block may appear. The incidence of a postdural puncture headache after an accidental wet tap with an epidural needle is more than 50%. After delivery of the fetus, the catheter should be removed. Intravenous and oral caffeinated beverages should be encouraged. Intravenous caffeine and oral analgesics may be used as well. If symptoms worsen (e.g., tinnitus, blurry vision, neck pain, difficulty sitting or standing), one should consider an epidural blood patch. Immediate relief occurs in almost 90% of patients on first attempt. Transient side effects include backache and neck pain. Second, an epidural catheter (20 gauge) can be inserted intrathecally for use as a continuous spinal catheter. After delivery, one can remove the catheter and follow the guidelines as listed earlier, or one can consider maintaining the intrathecal catheter in place for 24 hours to allow for an inflammatory reaction to develop around the intrathecal catheter. This inflammatory reaction may decrease the leakage of cerebrospinal fluid and thereby the incidence of postdural puncture headache.

Gaiser R. Postdural puncture headache. *Curr Opin Anaesthesiol.* 2006;19:249–253.

C.10. How would you manage total spinal anesthesia?

- High spinal anesthesia may occur several minutes after an epidural injection of local anesthetic. It is vitally important to communicate with the patient. Agitation, dyspnea, and difficulty speaking may herald the onset of total spinal anesthesia.
- Avoid aortocaval compression.
- Administer 100% oxygen to the mother.
- Provide positive pressure ventilation, preferably through an endotracheal tube.
- Monitor maternal BP, ECG recordings, and fetal heart rate.
- Support maternal circulation with intravenous fluids and ephedrine as needed. Do not hesitate to give epinephrine if needed.

Chestnut DH, ed. *Obstetric Anesthesia: Principles and Practice.* 4th ed. Philadelphia: Elsevier Mosby; 2009:462–463.

C.11. Should ergonovine be given to preeclamptic patients?

Preeclampsia is a relative contraindication to the use of ergot alkaloids because of the risk of inducing a hypertension crisis. In preeclamptic patients, uterine atony unresponsive to oxytocin may be treated with 15-methylprostaglandin $F_{2\alpha}$.

Chestnut DH, ed. *Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Elsevier Mosby; 2009:821.

Secher NJ, Arnsbro P, Wallin L. Haemodynamic effects of oxytocin and methyl ergometrine on the systemic and pulmonary circulations of pregnant anaesthetized women. *Acta Obstet Gynecol Scand*. 1978;57:97–103.

C.12. When and how would you give spinal anesthesia?

Spinal anesthesia may be used for cesarean delivery, even in a patient with severe preeclampsia. Hyperbaric bupivacaine 0.75% in a dose of 11.25 mg to 12 mg with or without fentanyl, 15 to 20 μg, or morphine, 100 to 200 μg, may be given.

Advantages of spinal anesthesia in severe preeclampsia include:

- Avoidance of general anesthesia and risks of difficulty with an edematous airway
- Elimination of risk of severe hypertensive response to laryngoscopy and endotracheal intubation, which can result in intracranial hemorrhage
- More reliable anesthesia than with an epidural anesthetic technique
- Smaller needle size than an epidural and therefore possibly less risk of trauma to epidural veins

One study by Aya et al. noted that the risk of hypotension was almost six times less in severely preeclamptic women than in healthy pregnant women receiving spinal anesthesia for elective cesarean section.

Aya AG, Mangin R, Vialles N, et al. Patients with severe preeclampsia experience less hypotension during spinal anesthesia for elective cesarean delivery than healthy parturients: a prospective cohort comparison. *Anesth Analg*. 2003;97:867–872.

Chestnut DH, ed. *Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Elsevier Mosby; 2009:993–995.

C.13. Discuss a general anesthesia technique for the patient with preeclampsia presenting for cesarean delivery.

- Aspiration prophylaxis. Acceptable methods include 30 mL of an oral nonparticulate antacid, and/or an H_2-blocker intravenously and possibly metoclopramide, 10 mg intravenously.
- Preoxygenation and denitrogenation with 100% oxygen through face mask
- Induction of anesthesia with cricoid pressure and sodium pentothal, 4 to 6 mg per kg
- Succinylcholine, 1.5 mg per kg, for effective intubation conditions
- Use a smaller endotracheal tube (6.0 or 6.5 mm internal diameter) because of airway edema.
- May consider use of nondepolarizing muscle relaxants for maintenance of neuromuscular block once the patient has demonstrated recovery from succinylcholine. Magnesium sulfate potentiates the effects of both depolarizing and nondepolarizing muscle relaxants.
- Use two-thirds of the minimum alveolar concentration of inhalation agent of the nonpregnant adult to ensure an adequate depth of anesthesia.
- Continue magnesium sulfate administration during intraoperative and postoperative periods.
- Consider arterial line placement before induction in patients with severe preeclampsia for continuous BP measurement. The transient but severe hypertension that accompanies tracheal intubation in preeclamptic women can significantly increase maternal intracranial pressure, with the attendant risks of cerebrovascular accident.
- Antihypertensive drugs can be given as required.

Chestnut DH, ed. *Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Elsevier Mosby; 2009:995–996.

C.14. What agents can you use to prevent hypertension during the induction of general anesthesia for cesarean delivery?

Before induction, labetalol, 5- to 10-mg increments, nitroglycerin (NTG), 50 to 100 μg increments; or sodium nitroprusside (SNP), 50-μg increments, can be used to attenuate the pressor response to laryngoscopy and intubation. Also, the short-acting opioid remifentanil can be used.

Chestnut DH, ed. *Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Elsevier Mosby; 2009:995–996.

C.15. What is HELLP syndrome?

HELLP syndrome is a severe form of preeclampsia characterized by hemolysis (*H*), elevated liver enzymes (*EL*), and low platelets (*LP*). It can occur antepartum or postpartum. Delivery represents the only definitive treatment of HELLP syndrome. HELLP syndrome is associated with maternal and neonatal morbidity and mortality. Hemolysis is defined by an abnormal peripheral blood smear and an increased bilirubin level (1.2 mg per dL or greater). Elevated liver enzymes are defined as an increased serum glutamic-oxaloacetic transaminase (aspartate aminotransferase) of at least 70 U per L and a lactate dehydrogenase level of more than 600 U per L. A low platelet count is defined as a count of less than 100,000 per mm^3. Patients with HELLP syndrome have a high incidence of serious maternal complications including disseminated intravascular coagulation, placental abruption, need for blood transfusion, pleural effusion, acute renal failure, and wound infection.

Audibert F, Friedman SA, Frangieh AY, et al. Clinical utility of strict diagnostic criteria for the HELLP (hemolysis, elevated liver enzymes, and low platelets) syndrome. *Am J Obstet Gynecol*. 1996;175:460–464.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone; 2008.

Sibai BM. The HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets): much ado about nothing. *Am J Obstet Gynecol*. 1990;162:311–316.

D. Postoperative Management

D.1. Discuss the postpartum management of preeclamptic patients.

- Provide adequate analgesia.
- Maintain strict intake/output for at least 24 hours postpartum or until diuresis develops.
- Continue magnesium sulfate for at least 24 hours postpartum or until evidence of diuresis.
- Maintain hemodynamic control with antihypertensives if necessary.

Chestnut DH, ed. *Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Elsevier Mosby; 2009:997.

CHAPTER 29

Breech Presentation, Fetal Distress, and Mitral Stenosis

Jill Fong

A 25-YEAR-OLD UNREGISTERED PRIMIGRAVIDA at 38 weeks of gestation presented to the labor room contracting. The patient had a history of rheumatic fever with no subsequent medical follow-up. On physical examination, she had a diastolic murmur and an opening snap. She reported having shortness of breath when climbing two flights of stairs. She was attached to an external fetal heart rate (FHR) monitor and tocodynamometer; recurrent variable decelerations without any beat-to-beat variability were noted. Simultaneously, the patient was found to have ruptured membranes, meconium-stained amniotic fluid, a fetal foot in her vagina, and a prolapsed umbilical cord. She was rushed to the operating room for an emergency cesarean section. Her blood pressure was 100/60 mm Hg; pulse rate, 100 beats per minute; respiratory rate, 18 breaths per minute.

A. Medical Disease and Differential Diagnosis

1. How are fetal lie, presentation, and position defined and determined?
2. What is the approximate frequency of the various lies and presentations at or near term?
3. What are the different types of breech presentation, and what is their incidence?
4. What is the cause of breech presentation?
5. What are the problems associated with breech presentation?
6. What is the usual obstetrical management for patients with breech presentation?
7. What is the incidence of heart disease in pregnancy?
8. What is the mortality rate associated with maternal cardiac disease?
9. What is the functional classification of heart disease by the New York Heart Association (NYHA)?
10. What are the cardiovascular changes of pregnancy?
11. What changes may normally occur in heart sounds during pregnancy?

12. What are the normal electrocardiographic and echocardiographic changes seen during pregnancy?
13. What causes rheumatic heart disease?
14. What are the physiologic consequences of mitral stenosis?
15. What are the ausculatory findings associated with mitral stenosis?
16. What may be seen on the electrocardiogram (ECG) in patients with mitral stenosis?
17. What are the echocardiographic findings associated with mitral stenosis?
18. What is the effect of the physiologic changes of pregnancy on patients with mitral stenosis?
19. If mitral stenosis is first recognized during pregnancy and symptoms develop, how would you treat the patient?
20. What are the determinants of fetal oxygenation?
21. What are the determinants of uterine blood flow?

B. Preoperative Evaluation and Preparation

1. How is fetal well-being assessed during labor?
2. How are FHR and maternal contractions monitored?
3. What is the normal FHR with beat-to-beat variability?
4. What are periodic decelerations?
5. How accurate is FHR monitoring in predicting fetal well-being?
6. In the fetus with a nonreassuring FHR pattern, what other modalities can be used to evaluate fetal well-being?
7. What is the significance of meconium-stained amniotic fluid?
8. What is meconium aspiration syndrome?
9. What are the usual noninvasive tests used to evaluate the pregnant cardiac patient?
10. What preoperative medications would you give this patient?

C. Intraoperative Management

1. What monitors would you use in this NYHA class II patient during her cesarean section?
2. When would you use invasive monitoring in a pregnant patient with cardiac disease?
3. What are the hemodynamic goals of intraoperative management of the pregnant patient with mitral stenosis?
4. What anesthetic technique would you use for emergency cesarean section?
5. What technique could you use for general anesthesia in this patient?
6. If you had unexpectedly been unable to intubate this patient, how would you have managed the airway?
7. Would this patient benefit from the use of β-blockers?
8. What is the effect of the inhalation agents on uterine contractility?
9. What is the Apgar scoring system?
10. What is the significance of Apgar scores?
11. At birth, what should be done to minimize an infant's risk of meconium aspiration syndrome?
12. The Apgar score of the newborn was 3 at 1 minute. How would you treat the newborn?
13. Blood gases are sent immediately after delivery. What are the normal values for umbilical vein and artery blood gases?

D. Postoperative Management

1. Immediately after the baby was delivered, the patient's oxygen saturation decreased. What is the differential diagnosis?

A. Medical Disease and Differential Diagnosis

A.1. How are fetal lie, presentation, and position defined and determined?

- Fetal lie describes the position of the long axis of the fetus in relative to the long axis of the mother. Longitudinal, transverse, and oblique lies exist. Longitudinal lies are either cephalic or pelvic (breech) depending on which fetal structure enters the maternal pelvis. Transverse lies are either back up or back down with the long axis of the fetus perpendicular (90 degrees) to the mother's long axis. An oblique lie results when the long axis of the fetus is at an acute angle to that of the mother. It is usually only transitory and converts to a transverse or longitudinal lie when labor begins.
- Presentation describes the part of the fetus that is lowermost in the pelvis: cephalic, breech, or shoulder. Cephalic presentations are further subdivided into vertex, brow, and face presentations.
- Position of the presenting part is described as a relationship between a certain pole of the fetal presenting part and the maternal surrounding pelvis.
- Fetal lie, presentation, and position can often be determined by manual pelvic and abdominal examination. Ultrasonography is also useful, particularly, when palpation is inconclusive, as can occur with multiple gestations, placenta previa, and hydramnios.

Cunningham FG, Leveno KJ, Bloom SL, et al., eds. *Williams Obstetrics*. 23rd ed. New York: McGraw-Hill; 2010:527.

A.2. What is the approximate frequency of the various lies and presentations at or near term?

Cephalic presentation, 97%; breech presentation, 3% to 4%; transverse lie, 0.3%; and face presentation, 0.5%.

Cunningham FG, Leveno KJ, Bloom SL, et al., eds. *Williams Obstetrics*. 23rd ed. New York: McGraw-Hill; 2010:527.

A.3. What are the different types of breech presentation, and what is their incidence?

- *Frank breech*: Both fetal lower extremities are flexed at the hips and extended at the knees. The incidence is approximately 60% (48% to 73%) of breech presentations.
- *Complete breech*: The knees are flexed, as are the hips. The incidence is approximately 10% (5% to 12%).
- *Incomplete or footling breech*: One or both hips are extended and a foot or knee hangs below the breech. The incidence is approximately 30% (12% to 38%).

Gabbe SG, Niebyl JR, Simpson JL, eds. *Obstetrics–Normal and Problem Pregnancies*. 5th ed. Philadelphia: Churchill Livingstone/Elsevier; 2007:436.

A.4. What is the cause of breech presentation?

The etiology of breech is unknown, but certain factors are associated with this presentation including prematurity, hydramnios, uterine relaxation associated with high parity, multiple fetuses, oligohydramnios, hydrocephaly, anencephaly, previous breech delivery, uterine anomalies, pelvic tumors, and cornual–fundal placenta implantation. A twofold increase in the incidence of breech presentation after a prior cesarean delivery was reported by Vendittelli et al.

Cunningham FG, Leveno KJ, Bloom SL, et al., eds. *Williams Obstetrics*. 23rd ed. New York: McGraw-Hill; 2010:527.

Venditelli F, Riviere O, Creen-Hebrert C, et al. Is a breech presentation at term more frequent in women with a history of cesarean delivery? *Am J Obstet Gynecol*. 2008; 198(5):521.e1.

A.5. What are the problems associated with breech presentation?

There is an increased incidence of prolapsed cord, perinatal morbidity and mortality resulting from difficult delivery, preterm delivery, fetal anomalies, placenta previa, and uterine anomalies.

Cunningham FG, Leveno KJ, Bloom SL, et al., eds. *Williams Obstetrics*. 23rd ed. New York: McGraw-Hill; 2010:529.

A.6. What is the usual obstetrical management for patients with breech presentation?

An external cephalic version can be attempted to convert the breech to a vertex presentation in patients who are candidates for vaginal deliveries. External cephalic version is often used in patients with breech presentation fetuses; however, the best time to attempt the version is unclear. Ylikorkula and Hartikainen-Sorri found that before 34 weeks' gestation, many breech infants will spontaneously convert to cephalic, and few will do so after that time. In general, external version should be considered in patients when a breech presentation is recognized prior to labor at or after 36 weeks' gestation. The reported success rates vary from 35% to 86%. A version success rate of 65% was reported by Zhang, and almost of all of the fetuses stayed in cephalic presentation. Successful version is more common in parous than nulliparous women, and more successful between 37 and 39 weeks than after 40 weeks. Tocolysis has been shown to be variably effective in improving version success rates. Epidural anesthesia during version has been shown by Schorr et al. and Mancuso et al. to improve the success rate of external cephalic version. While others have found no improvement in version success associated with neuraxial analgesia/anesthesia, Collaris and Oei found that maternal and fetal complications increased when conduction anesthesia had been used, and they concluded that the decreased maternal pain associated with these versions encouraged an overzealous application of force. If the version is successful, labor and vaginal delivery may proceed.

The 2006 recommendation from American College of Obstetricians and Gynecologists (ACOG) for breech delivery of the singleton fetus states "the decision regarding mode of delivery should depend on the experience of the health care provider," and "planned vaginal delivery of a term singleton breech fetus may be reasonable under hospital-specific protocol guidelines." Cesarean delivery is commonly used in the following circumstances: incomplete or footling breech, hyperextended fetal head, fetal macrosomia, unfavorable pelvic shape, severe fetal growth retardation, delivery needed in absence of spontaneous labor, healthy preterm fetus with maternal labor, previous perinatal death/trauma, maternal sterilization request, and lack of operator experience.

American College of Obstetricians & Gynecologists. Mode of term singleton breech delivery. Committee Opinion No. 340, July 2006.

Collaris RJ, Oei SG. External cephalic version: a safe procedure? A systematic review of version related risks. *Acta Obstet Gynecol Scand.* 2004; 83:511.

Cunningham FG, Leveno KJ, Bloom SL, et al., eds. *Williams Obstetrics.* 23rd ed. New York: McGraw-Hill; 2010:531, 539–540.

Gabbe SG, Niebyl JR, Simpson JL, eds. *Obstetrics–Normal and Problem Pregnancies.* 5th eds. Philadelphia: Churchill Livingstone/Elsevier; 2007:436.

Mancuso KM, Yancey MK, Murphy JA, et al. Epidural anesthesia for cephalic version: a randomized trial. *Obstet Gynecol.* 2000;95(5):648.

Schorr SJ, Speights SE, Rose EL, et al. A randomized trial of epidural anesthesia to improve external cephalic version success. *Am J Obstet Gynecol.* 1997;177:1133.

Skupski DW, Harrison-Restelli C, Dupont RB. External cephalic version: an approach with few complications. *Gynecol Obstet Invest.* 2003;56(2):83.

A.7. What is the incidence of heart disease in pregnancy?

The incidence of clinically significant cardiac disease has fallen to less than 1%. This decrease in incidence is due to the successful treatment of intrinsic cardiac disease and infections that cause cardiac disease. Congenital heart disease, not rheumatic heart disease, is now the major cause of heart disease in pregnancy in the developed world. Heart disease is the leading cause of death in women 25 to 44 years old according to the Centers for Disease Control and Prevention.

Chestnut DH, Polley LS, Tsen LC, et al., eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby/Elsevier; 2009:881.

Cunningham FG, Leveno KJ, Bloom SL, et al., eds. *Williams Obstetrics.* 23rd ed. New York: McGraw-Hill; 2010:531, 958.

Kung HC, Hoyert DL, Xu J, et al. Deaths: final data for 2005. *Natl Vital Stat Rep*. 2008;56(10):121.

A.8. What is the mortality rate associated with maternal cardiac disease?

Maternal mortality rate correlates well with the NYHA functional classifications. It is less than 1% in class I or II patients and between 5% and 15% in class III and IV patients. Patients with pulmonary hypertension, Eisenmenger syndrome, and severe Marfan syndrome have a high mortality rate regardless of functional class.

Chestnut DH, Polley LS, Tsen LC, et al., eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Mosby/Elsevier; 2009:881.

A.9. What is the functional classification of heart disease by the New York Heart Association (NYHA)?

The NYHA classification of a complete diagnosis of cardiovascular disease is not widely used now. The grading of dyspnea and/or fatigue resulting from heart failure is, however, often still classified using the old functional NYHA classification.

- *Class I* : no limitation of physical activity
- *Class II* : slight limitation of physical activity; symptoms with ordinary activity
- *Class III* : marked limitation of physical activity; symptoms with less than ordinary activity
- *Class IV* : unable to carry on any physical activity without discomfort; symptoms may be present at rest

On the basis of an analysis of 562 pregnant patients with heart disease, Siu et al. expanded on the NYHA classification and developed a system for predicting complications during pregnancy. Their predictors of cardiac complications included the following:

1. Prior heart failure, arrhythmia, transient ischemic attack, or stroke
2. A baseline NYHA III or IV classification or cyanosis
3. A left-sided heart obstruction defined as a mitral valve area less than 2 cm^2, aortic valve area less than 1.5 cm^2, or an echocardiographically demonstrated peak left ventricular outflow tract gradient exceeding 30 mm Hg
4. Less than 40% ejection fraction

With one of these factors, the risk of sustained arrhythmia, pulmonary edema, stroke, or cardiac death was increased, and if two or more factors existed, the risk was enhanced. Similarly, Stangl et al. found that pregnant patients with acquired and congenital cardiac disease were at increased risk of maternal and fetal morbidity and mortality if they had a left ventricular ejection fraction $< 50\%$, a NYHA class $> II$, a peak left ventricular outflow gradient > 60 mm Hg, or were cyanotic.

Cunningham FG, Leveno KJ, Bloom SL, et al., eds. *Williams Obstetrics*. 23rd ed. New York: McGraw-Hill; 2010:959–960.

Siu SC, Sermer M, Colman JM, et al. Prospective multicenter study of pregnancy outcomes in women with heart disease. *Circulation*. 2001;104:515.

Stangl V, Schad J, Gossing G, et al. Maternal heart disease and pregnancy outcome: a single-centre experience. *Eur J Heart Fail*. 2008;10:855.

A.10. What are the cardiovascular changes of pregnancy?

During the first trimester of pregnancy, the cardiac output increases to between 40% and 50% above the normal nonpregnant level and plateaus at approximately 28 weeks of gestation. It remains fairly stable until the stresses imposed by labor increase it further. The increase in cardiac output is due to a 30% increase in stroke volume and a 15% increase in heart rate. Blood pressure, however, is not elevated because peripheral vascular resistance decreases. Central venous pressure, pulmonary capillary wedge pressure, pulmonary artery diastolic pressure, and left ventricular stroke work index are unchanged when compared to nonpregnant values.

During labor, cardiac output increases approximately 15% with uterine contractions during the latent phase, 30% in the active phase, and 45% in the expulsive phase when compared to prelabor values. The greatest increase in cardiac output occurs immediately postpartum when it increases an average of 80% above prelabor values. Cardiac output and heart rate decline to prelabor values within 1 hour of delivery, and by approximately 24 hours, mean blood pressure and stroke volume return to their prelabor values. In the first 3 to 6 months after delivery, the cardiovascular changes of pregnancy resolve. It can take a year, however, for the residual effects of cardiovascular remodeling to subside.

Clark SL, Cotton DM, Lee LW, et al. Central hemodynamic assessment of normal term pregnancy. *Am J Obstet Gynecol*. 1989;161(6):1439.

Gabbe SG, Niebyl JR, Simpson JL, eds. *Obstetrics–Normal and Problem Pregnancies*. 5th ed. Philadelphia: Churchill Livingstone/Elsevier; 2007:57–62.

Ueland K, Novy MJ, Peterson EN, et al. Maternal cardiovascular dynamics, IV: the influence of gestational age on the maternal cardiovascular response to posture and exercise. *Am J Obstet Gynecol*. 1969;104:856–864.

Walters WAW, MacGregor WG, Hill M. Cardiac output at rest during pregnancy and the puerperium. *Clin Sci*. 1966;30:1–11.

A.11. What changes may normally occur in heart sounds during pregnancy?

In a study of 50 normal pregnant women at varying stages in pregnancy, a phonocardiographic study found that the first heart sound might have an exaggerated split with increased loudness of both components. In up to 84% of pregnant patients, a third heart sound is also evident. Functional systolic murmurs, which disappear shortly after delivery, occur in more than 90% of pregnant women. Soft transient diastolic murmurs occur in 18% of these women, and 10% have continuous murmurs apparently arising from the breast vasculature. These murmurs alone, therefore, are not indicative of organic heart disease. Similarly, venous distention, tachycardia, edema, and breathlessness may be seen with pregnancy and not be a sign of heart disease. Audible diastolic murmurs on auscultation are uncommon, however, and warrant further investigation.

Cutforth R, MacDonald CB. Heart sounds and murmurs in pregnancy. *Am Heart J.* 1966;71:741.

Fuster V, O'Rourke RA, Walsh RA, et al., eds. *Hurst's the heart*, 12th ed. New York: McGraw Hill, 2008:2192.

Gabbe SG, Niebyl JR, Simpson JL, eds. *Obstetrics–Normal and Problem Pregnancies*. 5th ed. Philadelphia: Churchill Livingstone/Elsevier; 2007:61.

A.12. What are the normal electrocardiographic and echocardiographic changes seen during pregnancy?

Normal pregnancy has no characteristic electrocardiographic change. Premature atrial and ventricular contractions can occur. The QRS axis may be deviated to the right during the first trimester but to the left in the third trimester. In lead III, inverted P waves and small Q waves may be seen that disappear with inspiration. Some ST-segment depression and flattening or inverting of the T waves may occur.

Normal echocardiographic findings include an increase in atrial diameters bilaterally. Left ventricular wall mass is increased. Left ventricular function is unchanged or slightly improved. The annuli of the pulmonary, tricuspid, and mitral valves dilate progressively, and term pregnant women may have mild tricuspid, pulmonic, and/or much more infrequently mitral regurgitation. A small pericardial effusion may develop as well.

Carruth JE, Mivis SB, Brogan DR, et al. The electrocardiogram in normal pregnancy. *Am Heart J*. 1981;102(6):1075.

Cunningham FG, Leveno KJ, Bloom SL, et al., eds. *Williams Obstetrics*. 23rd ed. New York: McGraw-Hill; 2010:959.

Desai DK, Moodley J, Naidoo D. Echocardiographic hemodynamics in normal pregnancy. *Obstet Gynecol*. 2004;104(1):20.

Fuster V, O'Rourke RA, Walsh RA, et al., eds. *Hurst's the heart*. 12th ed. New York: McGraw-Hill; 2008:2192.

Kametas N, McAuliffe F, Hancock J, et al. Maternal left ventricular mass and diastolic function during pregnancy. *Ultrasound Obstet Gynecol*. 2001;18:460.

A.13. What causes rheumatic heart disease?

Rheumatic heart disease may occur in patients who have had acute rheumatic fever, which is an autoimmune disease. The diagnosis of acute rheumatic fever is a clinical one, and the manifestations are extremely variable. There are no specific laboratory tests to confirm the diagnosis, and the exact pathogenetic mechanism is unknown. All cases of acute rheumatic fever follow a group A streptococcal upper respiratory tract infection. The diagnosis is made using the original Jones criteria and the 1992

American Heart Association committee update. In addition to the requirement of supporting evidence of an antecedent group A streptococcal tonsillopharyngitis infection, there are five major criteria: carditis, polyarthritis, Sydenham chorea, erythema marginatum, and subcutaneous nodules. Several minor criteria exist. The presence of one major and two minor or two major criteria are needed for the diagnosis.

Rheumatic fever usually first occurs in 5- to 15-year-old children. Rheumatic heart disease is the only long-term sequela of acute rheumatic fever. With the improved ability to prevent recurrent attacks, the prognosis of these patients has improved greatly. An individual's prognosis is related directly to the severity of cardiac involvement during the acute phase. On 10-year follow-up after acute rheumatic fever, only 6% of patients with no history of carditis had heart murmurs. Heart disease occurred, however, in 30%, 40%, and 68% of the patients who had apical systolic murmurs, basal diastolic murmurs, and pericarditis and/or congestive heart failure, respectively, during the initial attack. In temperate climate zones, such as in the United States and Europe, the time from an acute episode to the development of mitral stenosis (if it occurs) is about 15 to 20 years, and the progression from mild to severe mitral stenosis takes about 5 to 10 years. In tropical climates, the onset and progression are much more rapid. Mitral stenosis is the most common valvular lesion in women with a history of rheumatic heart disease. Mitral valve insufficiency and aortic valve stenosis and insufficiency can also occur in these patients.

Libby P, Bonow RO, Mann DL, et al., eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 8th ed. Philadelphia: Saunders/Elsevier; 2008:1651, 2079.

Mandell GL. *Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases*. 7th ed. Philadelphia: Churchill Livingstone; 2010:2611–2622.

A.14. What are the physiologic consequences of mitral stenosis?

The normal mitral valve orifice area is 4 to 6 cm^2. With mitral stenosis, the valve area is reduced. When the valve area reaches 2 cm^2, cardiovascular hemodynamics become impaired. When the valves cross-sectional area is between 1.0 and 1.5 cm^2, the mitral stenosis is classified as moderate. As the area decreases further to 1 cm^2, it is considered severe, and mean left atrial pressure increases to at least 25 mm Hg to maintain an adequate cardiac output. Left ventricular diastolic pressure is usually normal. Pulmonary venous and capillary pressures increase, leading to exertional dyspnea. If pulmonary capillary pressure exceeds blood oncotic pressure, pulmonary edema can develop. Pulmonary hypertension can result from elevated left atrial pressure and pulmonary arteriolar constriction. If severe pulmonary hypertension develops, right-sided heart failure can occur. Factors that may increase pulmonary pressure include tachycardia, increased cardiac output, and atrial fibrillation.

Brady K, Duff P. Rheumatic heart disease in pregnancy. *Clin Obstet Gynecol*. 1989;32:21.

Funai EF, Evans MI, Lockwood CJ. *High Risk Obstetrics: The Requisites in Obstetrics & Gynecology*. Philadelphia: Mosby/Elsevier; 2008:338, 367.

Libby P, Bonow RO, Mann DL, et al., eds. *Braunwald's heart disease: a textbook of cardiovascular Medicine*. 8th ed. Philadelphia: Saunders/Elsevier; 2008:1646.

A.15. What are the ausculatory findings associated with mitral stenosis?

The first heart sound is increased. There may be an opening snap heard along the left sternal border. A diastolic rumbling murmur is present at the mitral area and may be best heard with the patient in the left lateral decubitus position.

Bickley LS. *Bates' Guide to Physical Examination and History Taking*. 10th ed. Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins; 2009:386.

Fuster V, O'Rourke RA, Walsh RA, et al., eds. *Hurst's the Heart*. 12th ed. New York: McGraw Hill; 2008:1760.

A.16. What may be seen on the electrocardiogram (ECG) in patients with mitral stenosis?

There may be broadened diphasic P waves in lead V_1 with a larger negative terminal component that is indicative of left atrial enlargement. There may be signs of right ventricular hypertrophy. Atrial fibrillation may be present.

Dubin D. *Rapid Interpretation of EKGs*. 6th ed. Fort Myers, FL: Cover Publishing; 2000:249.

Libby P, Bonow RO, Mann DL, et al., eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 8th ed. Philadelphia: Saunders/Elsevier; 2008:1651.

A.17. What are the echocardiographic findings associated with mitral stenosis?

Two-dimensional (2D) echocardiography and Doppler ultrasonography are the mainstays of diagnosis and characterization of mitral stenosis. On 2D echo, the hallmark of mitral stenosis is thickening and restriction of motion of both mitral valve leaflets with the main process being fibrosis and fusion of the leaflets tips and proximal chordae. Early on due to inflammation and leaflet tip thickening that restricts tip but not leaflet motion, a characteristic "doming" of the valve occurs during diastole and the anterior leaflet has a "hockey-stick" configuration (Fig. 29.1). As the stenosis progresses, the body of the leaflet may become involved, and calcification can occur within the leaflets and on the subvalular apparatus including the chordae and papillary muscle tips. Left atrial enlargement can be seen. Pulmonary valve motion abnormalities and right ventricular enlargement may

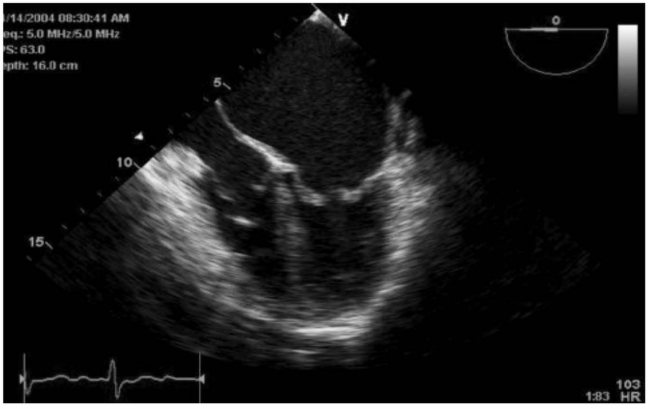

Figure 29.1 Two-dimensional echocardiography of the mitral valve showing severe mitral stenosis with the typical "hockey-stick" appearance.

signify pulmonary hypertension. In addition to reduced excursion and thickening of the leaflets, M-mode echocardiography shows a decrease in the closure rate of the anterior mitral leaflet during early diastole; this results in a reduced E-F slope. M-mode and 2D echocardiography do not reliably predict the severity of mitral stenosis. In addition to determining the anatomic extent and severity of the lesion, Doppler echocardiography can assess the physiologic significance of the lesion. Doppler studies can provide an estimate of valve area that is within ± 0.4 cm^2 of those obtained by cardiac catheterization. During pregnancy, however, mitral valve area calculations by Doppler may be inaccurate. Transesophageal echocardiography is helpful in assessing atrial thrombi.

Libby P, Bonow RO, Mann DL, et al., eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 8th ed. Philadelphia: Saunders/Elsevier; 2008:1650.

Rokey R, Hsu HW, Moise KJ, et al. Inaccurate noninvasive mitral valve area calculation during pregnancy. *Obstet Gynecol*. 1994;84:950.

A.18. What is the effect of the physiologic changes of pregnancy on patients with mitral stenosis?

The increased physiologic cardiovascular load of pregnancy can cause patients to deteriorate and advance from one NYHA classification to another. Hameed et al. found that more than half of NYHA class I and II patients with mitral stenosis had worsening clinical symptomatology during pregnancy. The incidence of maternal and fetal complications was related to the severity of the mitral stenosis. Similarly, Silversides et al. found the incidence of maternal cardiac complications with mild mitral stenosis to be lower (26%) than those occurring with moderate (38%) and severe (67%) disease. Maternal mortality is low, although isolated deaths have been reported in parturients with NYHA III and IV classified mitral stenosis .

Chestnut DH, Polley LS, Tsen LC, et al., eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Mosby/Elsevier; 2009:893.

Hameed A, Karaalp IS, Tummala PP, et al. The effect of valvular heart disease on maternal and fetal outcome of pregnancy. *J Am Coll Cardiol*. 2001;37(3):893–899.

Silversides CK, Colman JM, Sermer M, et al. Cardiac risk in pregnant women with rheumatic mitral stenosis. *Am J Cardiol*. 2003;91(11):1382–1385.

A.19. If mitral stenosis is first recognized during pregnancy and symptoms develop, how would you treat the patient?

Heart rate reduction and a decreased left atrial pressure are the standard therapeutic goals for women with moderate to severe mitral stenosis. Therefore, β-adrenergic receptor blockade is the cornerstone of medical therapy in the symptomatic patient. It is useful in preventing tachycardia and prolonging diastolic filling time, which can result in a marked improvement of symptoms. Atrial fibrillation or flutter should be treated aggressively; a rapid ventricular response compromises diastolic flow time and can lead to pulmonary edema. Emergency treatment includes digoxin, β-adrenergic receptor blockade, and/or cardioversion if needed. Atrial fibrillation not only increases the risk of pulmonary edema, but it also increases the likelihood of a thromboembolic event. Salt restriction and cautious use of diuretics can decrease left atrial pressure by decreasing blood volume. Avoidance of hypovolemia and decreased uteroplacental perfusion are essential.

If symptoms are uncontrolled by medical therapy, the mitral valve should be repaired or replaced. Percutaneous balloon valvuloplasty can be done using echocardiography or with appropriate radiation shielding of the fetus if radiographic imaging is required. For those with severe mitral stenosis, valve area less than 1 cm^2, a surgical commissurotomy or valve replacement is well tolerated by the mother, but fetal loss exceeds 10%.

Chambers CE, Clark SL. Cardiac surgery during pregnancy [Review]. *Clin Obstet Gynecol*. 1994;37:316–323.

Esteves CV, Auristela IOR, Braga SLN, et al. Effectiveness of percutaneous balloon mitral valvotomy during pregnancy. *Am J Cardiol*. 1991;68:930–934.

Libby P, Bonow RO, Mann DL, et al., eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 8th ed. Philadelphia: Saunders/Elsevier; 2008:1650.

A.20. What are the determinants of fetal oxygenation?

Fetal oxygenation is dependent on uteroplacental blood flow, oxygen-carrying capacity, oxygen affinity, arterial oxygen tension, placental diffusion capacity, placental vascular geometry, and placental oxygen consumption.

Cunningham FG, Leveno KJ, Bloom SL, et al., eds. *Williams Obstetrics*. 23rd ed. New York: McGraw-Hill; 2010:85–86.

Datta S, Kodali BS, Segal S. *Obstetric Anesthesia Handbook*. 5th ed. New York: Springer; 2010:66–68.

A.21. What are the determinants of uterine blood flow?

Uterine blood flow is derived from the Ohm's law, which states that pressure equals flow multiplied by resistance. Therefore, uterine blood flow is shown as follows:

$$\text{Uterine blood flow} = \frac{\text{uterine artery pressure} - \text{uterine venous pressure}}{\text{uterine artery resistance}}$$

Normally, 10% of maternal cardiac output goes to the uterus. Of this, the placenta receives 80%, and the myometrium receives the rest. Uterine blood flow is directly related to blood pressure; the uterine vessels do not autoregulate.

Datta S, Kodali BS, Segal S. *Obstetric Anesthesia Handbook*. 5th ed. New York: Springer; 2010:65.

Gabbe SG, Niebyl JR, Simpson JL, eds. *Obstetrics–Normal and Problem Pregnancies*. 5th ed. Philadelphia: Churchill Livingstone/Elsevier; 2007:32.

B. Preoperative Evaluation and Preparation

B.1. How is fetal well-being assessed during labor?

Fetal well-being is dependent on an intact uteroplacental unit. Simultaneous monitoring of FHR and uterine contractions aids in the detection of fetal distress.

B.2. How are FHR and maternal contractions monitored?

FHR can be monitored noninvasively using the Doppler technique or invasively using a fetal scalp electrode. Uterine contractions may be monitored noninvasively by a tocodynamometer, which measures the tightening of maternal abdominal muscles, or invasively by a transcervical pressure catheter hooked to a strain gauge.

Cunningham FG, Leveno KJ, Bloom SL, et al., eds. *Williams Obstetrics*. 23rd ed. New York: McGraw-Hill; 2010:410, 437.

B.3. What is the normal FHR with beat-to-beat variability?

Interpretation of FHR patterns can be confusing because of the lack of uniformity on definitions and nomenclature. During a 10-minute tracing segment, the baseline FHR is the approximate mean rate rounded to 5 beats per minute increments. In the third trimester, the normal mean baseline FHR is 120 to 160 beats per minute with beat-to-beat variability. Internationally, some recommend that 110 beats per minute be the lower limit of normal. A baseline FHR <110 beats per minute is termed *bradycardia* and >160 beats/min is called *tachycardia*. Normal beat-to-beat variability is 6 to 25 beats per minute.

Cunningham FG, Leveno KJ, Bloom SL, et al., eds. *Williams Obstetrics*. 23rd ed. New York: McGraw-Hill; 2010:413, 415.

B.4. What are periodic decelerations?

Periodic FHR patterns refer to changes in baseline FHR in relation to uterine contractions. An acceleration is an increase and a deceleration is a decrease in FHR from its baseline. In the United States, periodic decelerations in FHR fall into the following three categories—early, late, or variable—depending on their shape and timing with respect to maternal contractions (Fig. 29.2).

- Early, or type 1, decelerations are uniform FHR decreases that coincide with the onset, peak, and end of uterine contraction. This is a vagal response caused by fetal head compression and is usually not associated with fetal hypoxia.
- Late, or type 2, decelerations are a gradual decrease in FHR that begins after the onset of a contraction and lasts beyond the end of the contraction. They can indicate uteroplacental insufficiency, and require prompt evaluation and treatment.
- Variable, or type 3, decelerations occur variably and usually abruptly in relationship to contractions. They usually result from fetal blood pressure changes due to umbilical cord compression or changes in fetal oxygenation. Significant variable decelerations are defined by the ACOG as those that decrease to < 70 beats per minute and last longer than 60 seconds.

A prolonged deceleration is an isolated deceleration from baseline that lasts 2 or more minutes but less than 10 minutes. These are difficult to interpret, and management is based on bedside clinical judgment.

American College of Obstetricians and Gynecologists. Fetal heart rate patterns: Monitoring, interpretation, and management. *Technical Bulletin No. 207*, July 1995.

American College of Obstetricians and Gynecologists. Intrapartum fetal heart rate monitoring. *Practice Bulletin No. 70*, December, 2005.

Cunningham FG, Leveno KJ, Bloom SL, et al., eds. *Williams Obstetrics*. 23rd ed. New York: McGraw-Hill; 2010:420–424.

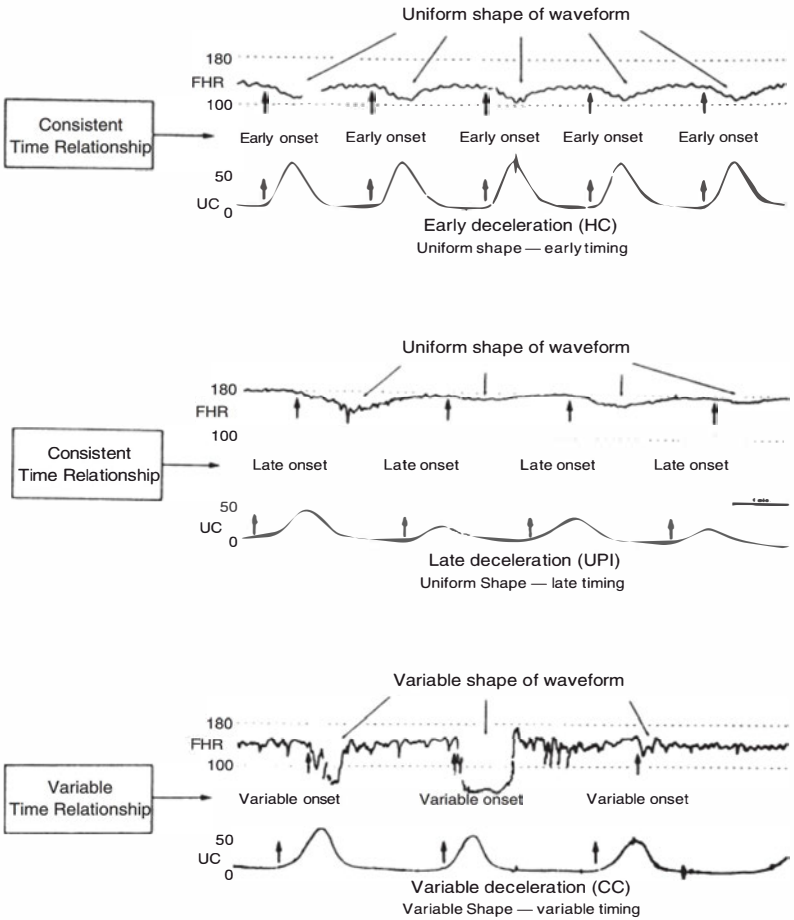

Figure 29.2 Fetal heart rate decelerations in relation to the time of onset of uterine contractions. (From Hon EH. *An Atlas of Fetal Heart Rate Patterns.* New Haven: Harty Press; 1968, with permission.)

B.5. How accurate is FHR monitoring in predicting fetal well-being?

Uncertainty about diagnosing fetal distress from FHR patterns has given rise to the descriptions of these patterns as reassuring or nonreassuring. After more than 40 years of FHR pattern interpretation, there is finally some evidence emerging that certain combinations can be used meaningfully to identify normal and severely abnormal fetuses. Normal FHR patterns include a baseline rate of 110–160 beats per minute, moderate beat-to-beat variability, and no late or variable decelerations; early decelerations and accelerations may or may not be present. Abnormal FHR patterns have absent baseline FHR variability and recurrent late decelerations, recurrent variable decelerations, or bradycardia. Sinusoidal patterns are also abnormal. *Reduced beat-to-beat variability is generally believed to be the single most reliable sign of fetal compromise.* True fetal distress patterns seem to be those where there is no beat-to-beat variability in conjunction with severe decelerations, persistent baseline

rate changes, or both. FHR patterns that do not fall into the aforementioned classifications of normal or abnormal represent an appreciable fraction of nonreassuring FHR tracings. These fetal assessments are subjective clinical judgments and are inevitably and knowingly open to imperfection. Management options depend upon whether or not the cause of the fetal insult can be identified and corrected.

Cunningham FG, Leveno KJ, Bloom SL, et al., eds. *Williams Obstetrics*. 23rd ed. New York: McGraw-Hill; 2010:429–431.

Low JA, Mc Grath MJ, Marshall SJ, et al. The relationship between antepartum fetal heart rate, intrapartum fetal heart rate, and fetal acid-base status. *Am J Obstet Gynecol*. 1986;154(4):769–776.

Macones GA, Hankins GD, Spong CY, et al. The 2008 National Institute of Child Health and Human Development Workshop report on electronic fetal monitoring. Update on definitions, interpretations, research guidelines. *Obstet Gynecol*. 2008;112:661

Paul RH, Suidan AK, Yeh S-Y, et al. Clinical fetal monitoring, VII: the evaluation and significance of intra-partum baseline FHR variability. *Am J Obstet Gynecol*. 1975;123(2):206–210.

B.6. In the fetus with a nonreassuring FHR pattern, what other modalities can be used to assess fetal well-being?

Intrapartum fetal stimulation and fetal scalp capillary blood pH are additional methods to assess fetal well-being. In the fetus with a nonreassuring FHR tracing, any spontaneous or induced (scalp or vibroacoustic stimulation) FHR accelerations may indicate the absence of acidosis but are less than perfect. Fetal capillary scalp pH is now uncommonly used. According to the ACOG, fetal outcome cannot be predicted by either normal or abnormal scalp pH results. Currently, fetal electrocardiography is still being investigated while fetal pulse oximetry has been abandoned. In a parturient with a breech fetus, any technique that requires access to the fetal head would not be applicable.

Cunningham FG, Leveno KJ, Bloom SL, et al., eds. *Williams Obstetrics*. 23rd ed. New York: McGraw-Hill; 2010:427–429.

Goodwin TM, Milner-Masterson L, Paul RH. Elimination of fetal scalp blood sampling on a large clinical service. *Obstet Gynecol*. 1994;83:971.

Yeoman ER, Hauth JC, Gilstrap LC III et al. Umbilical cord pH, P_{CO_2} and bicarbonate following uncomplicated term vaginal deliveries. *Am J Obstet Gynecol*. 1985;151:798.

B.7. What is the significance of meconium-stained amniotic fluid?

Although meconium staining occurs in 12% to 22% of all deliveries, most of the infants are not depressed; there is a high false-positive rate and low sensitivity for acidemia. The physiology of meconium passage and its adverse sequelae are incompletely understood. Three theories have been suggested to explain the passage of meconium by the fetus, and the wide differences in the proposed theories may help explain the tenuous connection between meconium detection and infant mortality. The pathologic explanation proposes that in response to hypoxia, the fetus passes meconium and that meconium, therefore, signals fetal compromise. Alternatively, in utero passage of meconium may indicate normal gastrointestinal tract maturation under neural control. A third alternative suggests that passage of meconium follows vagal stimulation from common but transient umbilical cord entrapment and resultant peristalsis.

Ramin et al. suggest meconium becomes an environmental hazard when fetal acidemia occurs rather than meconium release being solely a marker of preexisting fetal compromise. Importantly, because acidemia occurs acutely, meconium aspiration is unpredicatable and likely unpreventable. Greenwood et al. looked at women with clear amniotic fluid and emphasized that clear fluid is an unreliable sign of fetal well-being.

Evidence is accumulating that many infants with meconium aspiration syndrome have suffered hypoxia before birth. Blackwell et al. found that 60% of the infants with meconium aspiration syndrome had umbilical artery blood pH greater than or equal to 7.20; this suggests that this syndrome was unrelated to the neonates' condition at delivery. Meconium aspiration syndrome is more likely when meconium is thick, the pregnancy is post term, or the fetus is growth restricted.

Blackwell SC, Moldenhauer J, Hassan SS, et al. Meconium aspiration syndrome in term neonates with normal acid-base status at delivery: is it different?. *Am J Obstet Gynecol*. 2001;184:1422.

Cunningham FG, Leveno KJ, Bloom SL, et al., eds. *Williams Obstetrics*, 23rd ed. New York: McGraw-Hill, 2010:431–432.

Greenwood C, Lalchandani S, MacQuillan K, et al. Meconium passed in labor: how reassuring is clear amniotic fluid? *Obstet Gynecol*. 2003;102:89.

Ramin KD, Leveno KJ, Kelly MS, et al. Amniotic fluid meconium: a fetal environmental hazard. *Obstet Gynecol*. 1996;87:181.

B.8. What is meconium aspiration syndrome?

Of the 10% to 15% of births with meconium-stained amniotic fluid, 5% of the infants develop meconium aspiration pneumonia. Of these infants, 30% require mechanical ventilation, and 3% to 5% may die. Meconium inactivates surfactant.

Meconium aspiration syndrome is characterized by respiratory distress with a marked mismatch of ventilation to perfusion. Within 72 hours, the condition often improves, but when assisted ventilation is required, it may be severe and has a high associated mortality. Pneumothorax and/or pneumomediastinum are complications. With severe disease, pulmonary hypertension leading to persistent fetal circulation can occur.

Kliegman RM, Behrman RE, Jensen HB, et al., eds. *Nelson Textbook of Pediatrics*. 18th ed. Philadelphia: Saunders/Elsevier; 2007:742.

B.9. What are the usual noninvasive tests used to evaluate the pregnant cardiac patient?

Physical examination, exercise tolerance test, ECG, pulse oximeter oxygen saturation, Holter monitoring, and echocardiography with Doppler flow studies may all be useful in evaluating these patients. Cardiac magnetic resonance imaging is generally safe in pregnant women, but contrast dye should not be used. Tests using radiation should be avoided unless absolutely necessary. If a radiologic test is needed, delaying it until as late as possible in the pregnancy and protective fetal radiation shielding would be best. The risk of fetal anomalies is low with less than 5 rads of radiation exposure. Radiation exposure with a chest radiograph is approximately 20 millirads and with a radionuclide scan is about 40 millirads.

Fuster V, O'Rourke RA, Walsh RA, et al., eds. *Hurst's the Heart*. 12th ed. New York: McGraw-Hill; 2008:2192.

B.10. What preoperative medications would you give this patient?

Recommendations for antibiotic prophylaxis against endocarditis are dependent on the cardiac lesion and the procedure being performed. Prophylaxis has been overused. As recommended by the American Heart Association and endorsed by the ACOG, prophylaxis for bacterial endocarditis should be administered intrapartum to women at risk only in the presence of suspected bacteremia or active infection. In patients with acquired valvular dysfunction, endocarditis prophylaxis is not recommended for cesarean section or uncomplicated vaginal delivery. Only a few antibiotic regimens are recommended by the ACOG for prophylaxis if needed. Ampicillin 2 g intravenously (IV), cefazolin 1 g IV, or ceftriaxone 1 g IV should be given 30 to 60 minutes before the procedure. If the patient has penicillin allergy, clindamycin 600 mg IV should be given. If enterococci infection is suspected, vancomycin is recommended.

However, prophylactic antibiotics are given to patients having cesarean sections to prevent postcesarean section endomyometritis and wound infections. In the past, the antibiotic was given after cord clamping. Recently, however, the ACOG and the American Academy of Pediatrics, in a joint publication, have stated that "an antibiotic before the procedure [cesarean delivery] has been demonstrated to be more effective than administration immediately after umbilical cord clamping." They do not explicitly recommend preincision administration of antibiotic or use of an extended-spectrum regimen for endocarditis prophylaxis. However, in a comprehensive review, Tita et al. suggest using either cefazolin alone before surgical incision or an extended-spectrum regimen after cord clamp seems to reduce postcesarean maternal infection.

Pregnant patients are considered to be at an increased risk for aspiration of gastric contents. Gastric fluid volume and pH are not different in the pregnant patient versus their nonpregnant counterparts. Pregnancy itself may not decrease gastric emptying, but during labor, gastric motility does decrease. The increased risk is thought to be due to the parturient's decrease in lower esophageal sphincter tone, changes in the gastroesophageal junction angle, and an increased risk of having difficulty with intubation. Based on the chemical and physical nature of the aspirate and the volume, the risk of aspiration pneumonitis exists. With a nonparticulate aspirate, historically, patients were considered to be at risk for aspiration pneumonitis if greater than 0.4 mL/kg of fluid with a pH of less than 2.5 was aspirated. The volume guideline has been called into question. The goal of prophylactic therapy, however, remains the same. Ideally, the pH level should be greater than 2.5, and potential volume of the aspirate should be minimized. Although the exact time at which the risk increases is unclear, it seems prudent to consider the pregnant patient to be at increased risk for aspiration of gastric contents after 16 to 20 weeks' gestation. In this patient for emergency cesarean, an oral nonparticulate antacid such as 15 to 30 mL of 0.3 M sodium citrate given immediately before induction reduces the risk of developing aspiration pneumonitis. Ranitidine, cimetidine, and metoclopramide may also decrease this risk but require more time to be effective.

American College of Obstetricians and Gynecologists. Antibiotic prophylaxis for infective endocarditis. Committee Opinion No. 421. November 2008.

Chestnut DH, Polley LS, Tsen LC, et al., eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Mosby/Elsevier; 2009:24, 637, 647.

Cunningham FG, Leveno KJ, Bloom SL, et al., eds. *Williams Obstetrics*. 23rd ed. New York: McGraw-Hill; 2010:974.

Smaill F, Hofmeyr GJ. Antiobiotic prophylaxis for cesarean section. *Cochrane Database Syst Rev*. 2005;1.

Tita AJ, Rouse DJ, Blackwell S, et al. Emerging concepts in antibiotic prophylaxis for cesarean section: a systematic review. *Obstet Gynecol*. 2009;113(3):675–682.

C. Intraoperative Management

C.1. What monitors would you use in this functional NYHA class II patient during her cesarean section?

Pregnant cardiac patients should be monitored with an ECG, blood pressure monitoring, pulse oximetry, temperature monitor, and urinary catheter. In addition, end-tidal carbon dioxide, bispectral index, and neuromuscular blockade monitoring is recommended if general anesthesia is used.

C.2. When would you use invasive monitoring in a pregnant patient with cardiac disease?

NYHA class I and II patients do not routinely require invasive hemodynamic monitoring. However, the paturient in class III or IV is usually monitored with a pulmonary artery catheter. An arterial line may be placed if serial blood gas determinations and/or continuous blood pressure monitoring seems warranted. The hemodynamic monitoring should be continued for at least 24 hours postdelivery since the sudden increase in preload immediately after delivery can precipitate pulmonary edema.

Cunningham FG, Leveno KJ, Bloom SL, et al., eds. *Williams Obstetrics*. 23rd ed. New York: McGraw-Hill; 2010:966.

Funai EF, Evans MI, Lockwood CJ. *High Risk Obstetrics: The Requisites in Obstetrics & Gynecology*. Philadelphia: Mosby/Elsevier; 2008:338, 359.

C.3. What are the hemodynamic goals of intraoperative management of the pregnant patient with mitral stenosis?

- Avoid tachycardia.
- Maintain sinus rhythm.
- Avoid marked decrease in systemic vascular resistance.
- Avoid marked increase in central blood volume.
- Avoid increase in pulmonary vascular resistance.

Increased heart rate should be avoided because decrease in the amount of diastolic time for blood to flow across the stenotic mitral valve can lead to pulmonary edema and a decreased cardiac output. Atrial fibrillation with a rapid ventricular response similarly can result in cardiac decompensation, and the loss of atrial contraction is detrimental. Marked decrease in systemic vascular resistance should be avoided because compensatory increase in heart rate can result. Elevation of pulmonary vascular resistance, as can occur with hypercarbia, hypoxia, and acidosis, is poorly tolerated by these patients.

Datta S, Kodali BS, Segal S. *Obstetric Anesthesia Handbook*. 5th ed. New York: Springer; 2010:261.

C.4. What anesthetic technique would you use for this emergency cesarean section?

The choices of anesthetic techniques for cesarean section are regional, spinal or epidural, or general anesthesia. In this case, a general anesthetic would be the anesthetic of choice. General anesthesia has a rapid onset, which is necessary because of the abnormal FHR tracing and the inability to free the compressed prolapsed umbilical cord. In addition, if the patient has not been adequately hydrated with an IV crystalloid

solution before a rapid regional anesthetic induction, the resulting decrease in systemic vascular resistance, hypotension, and reflex tachycardia might exacerbate fetal distress and lead to maternal cardiac decompensation in the patient with mitral stenosis. In the nonemergent setting, patients with mitral stenosis do well with epidural anesthesia for their vaginal delivery or cesarean section. Combined spinal–epidural analgesia has also been used successfully in these patients during vaginal delivery.

Chestnut DH, Polley LS, Tsen LC, et al., eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Mosby/Elsevier; 2009:894.

C.5. What technique could you use for general anesthesia in this patient?

- IV crystalloid solution through a large-bore cannula (if not already present) should be used.
- Place the patient on the table in the supine position with left lateral tilt to avoid aortocaval compression.
- Preoxygenate the mother and place monitors on her quickly. Preoxygenation may be accomplished by allowing her to breathe 100% oxygen by face mask for 3 to 5 minutes or to take four maximally deep inspirations if time is limited.
- After a team "time-out" and abdominal preparation and draping, perform a rapid sequence induction using thiopental sodium, 4 mg per kg, and succinylcholine, 1 mg per kg. Ketamine should be avoided because it could increase heart rate. Pregnant women do not experience severe fasciculations; therefore, a defasciculatory dose of nondepolarizing muscle relaxant is not recommended. Depending on the severity, mitral stenosis patients may benefit from a β-adrenergic receptor antagonist, such as esmolol, or a modest dose of opioid before or during induction of general anesthesia. Remember to inform the neonatologist in the delivery room about the medications that the mother has received. If hypotension occurs, phenylephrine, not ephedrine, would be the vasopressor of choice because it does not cause tachycardia.
- Endotracheal intubation: Mucosal swelling and capillary engorgement can make intubation more difficult. A smaller endotracheal tube, such as a 7-mm internal diameter tube, should be used. The value of using cricoid pressure has been questioned. Classically, cricoid pressure is maintained until the endotracheal tube cuff is inflated and the position is checked. In human cadavers, cricoid pressure effectively prevented regurgitation with gastric pressures as high as 50 to 94 cm H_2O. Smith et al. found that cricoid pressure in awake volunteers led to airway displacement and did not reliably produce midline esophageal compression. This may limit its protective effect against passive reflux and make intubation more difficult.
- Maintenance of anesthesia before the baby is delivered involves the following: N_2O with at least 50% oxygen, volatile anesthetic agent (e.g., 1% sevoflurane), and muscle relaxant as needed (vecuronium, cisatracurium, or rocuronium). Isoflurane and desflurane probably should be avoided in this patient because they may cause tachycardia. Eucapnea should be maintained.
- Maintenance of anesthesia after the baby is delivered no longer requires fetal consideration. A narcotic technique can be implemented using, for instance, fentanyl, midazolam, muscle relaxant, nitrous oxide, and oxygen.
- After the delivery of newborn, any bolus administration of oxytocin, methylergonovine or 15-methyl prostaglandin F2-α can increase pulmonary vascular resistance.
- Tracheal extubation is done after her protective laryngeal reflexes have returned and the patient has regained consciousness.

American Society of Anesthesiologists Task Force on Obstetric Anesthesia. Practice guidelines for obstetric anesthesia: an updated report by the American Society of Anesthesiologists Task Force on Obstetric Anesthesia. *Anesthesiology*. 2007;106(4):843–63.

Chestnut DH, Polley LS, Tsen LC, et al., eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Mosby/Elsevier; 2009:544.

Fanning GL. The efficacy of cricoid pressure in regurgitation of gastric contents. *Anesthesiology*. 1970;32:553.

Norris MC, Dewan DM. Preoxygenation for cesarean section. A comparison of two techniques. *Anesthesiology*. 1985;62:827.

Smith KJ, Dobranowski J, Yip G, et al. Cricoid pressure displaces the esophagus: an observational study using magnetic resonance imaging. *Anesthesiology*. 2003;99(1):60.

Thind GS, Bryson THL. Single dose suxamethonium and muscle pain in pregnancy. *Br J Anaesth*. 1983;55:743.

C.6. If you had unexpectedly been unable to intubate this patient, how would you have managed the airway?

Figure 29.3 shows one way to deal with the failed intubation in the obstetric patient with an unrecognized difficult airway. However, other anesthetic techniques may be used. For instance, some would let the patient breathe spontaneously, and others would administer muscle relaxants while continuing mask ventilation. Additionally, some prefer video versus direct laryngoscopy for additional intubation attempts. Remember that like face mask ventilation, the laryngeal mask airway does not prevent aspiration. The mother's life should not be endangered to deliver a distressed fetus. Calling for help promptly when difficulties arise is wise.

American Society of Anesthesiologists Task Force on Management of the Difficult Airway. Practice guidelines for the management of the difficult airway. *Anesthesiology*. 2003; 98(5):1269–1277.

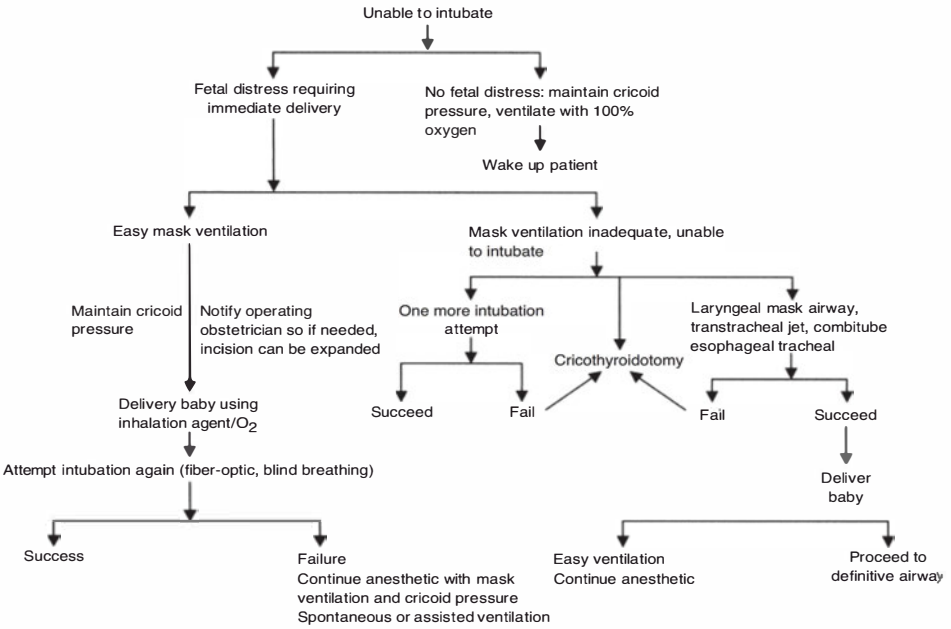

Figure 29.3 Algorithm for management of difficult intubation. If the surgeon infiltrates region with local anesthetic, it will decrease your general anesthetic requirement.

American Society of Anesthesiologists Task Force on Obstetric Anesthesia. Practice guidelines for obstetric anesthesia: an updated report by the American Society of Anesthesiologists Task Force on Obstetric Anesthesia. *Anesthesiology*. 2007;106(4):843–863.

Barker P, Langeton JA, Murphy PJ, et al. Regurgitation of gastric contents during general anesthesia using the laryngeal mask airway. *Br J Anaesth*. 1992;69:314.

C.7. Would this patient benefit from the use of β-blockers?

Since this patient is asymptomatic, β-blockade is unnecessary. Should compromising tachycardia occur, β-blockade with drugs such as propanolol, atenolol, or esmolol may be useful, as may digoxin or cardioversion depending on her dysrhythmia. Al Kasab et al. have shown that pregnant patients with symptomatic mitral stenosis who receive β-blockade with propanolol or atenolol to attenuate tachycardia have a significant decrease in the incidence of pulmonary edema with no adverse neonatal side effects.

Al Kasab SM, Sabag T, Zaibag MA, et al. β-Adrenergic receptor blockage in the management of pregnant women with mitral stenosis. *Am J Obstet Gynecol*. 1990;163:37.

C.8. What is the effect of the inhalation agents on uterine contractility?

If less than one minimum alveolar concentration of a potent volatile inhalation agent such as isoflurane or sevoflurane is used, there is no increase in blood loss or decrease in uterine contractility, because at these low concentrations, the uterus still responds to oxytocin. At higher concentrations, the uterine contractility is decreased and blood loss is increased.

Munson ES, Embro WJ. Enflurane, isoflurane and halothane and isolated human uterine muscle. *Anesthesiology*. 1977;46:11.

Tjeuw MTB, Yao FS, Van Poznak A. Depressant effects of anesthetics on isolated human gravid and nongravid uterine muscle. *Chinese Med J*. 1986;99(3):235–242.

Warren TM, Datta S, Ostheimer GW, et al. Comparison of the maternal and neonatal effects of halothane, enflurane and isoflurane for cesarean delivery. *Anesth Analg*. 1983;62:516.

C.9. What is the Apgar scoring system?

The Apgar scoring system is used in the delivery to assess the neonate's condition at 1 minute and 5 minutes. Each of five categories is given a rating of 0 to 2, and the final score at each time is the sum of the individual category scores. Ten points is the best possible neonatal Apgar score (Table 29.1).

Apgar V. A proposal for a new method of evaluation of the newborn infant. *Curr Res Anesth Analg*. 1953;32:260.

C.10. What is the significance of Apgar scores?

Overall, Apgar scores qualitatively measure basic neurologic reflexes and correlate with generalized neonatal depression. They only loosely correlate with acidosis and asphyxia. Apgar scores aid in predicting mortality but poorly predict morbidity; the longer the Apgar score is low, the higher the neonatal mortality.

Table 29.1 Apgar Scoring System

MNEMONIC	SIGN	SCORE 0	1	2
A	Appearance (color)	Blue, pale	Body pink, extremities blue	Pink
P	Pulse	Absent	<100/ min	>100/ min
G	Grimace (reflex irritability; response to catheter in the nose)	Absent	Grimace	Cough, sneeze
A	Activity (muscle tone)	Limp	Some extremity flexion	Active motion
R	Respiratory effect	Absent	Slow, irregular	Good cry

Glodenberg RL, Huddelston JF, Nelson KG. Apgar scores and umbilical arterial pH in preterm newborn infants. *Am J Obstet Gynecol.* 1984;149(6):651.

Low JA, Mc Grath MJ, Marshall SJ, et al. The relationship between antepartum fetal heart rate, intrapartum fetal heart rate, and fetal acid-base status. *Am J Obstet Gynecol.* 1986;154(4):769.

Silverman F, Suidan J, Wasserman J, et al. The Apgar score: is it enough? *Obstet Gynecol.* 1985;66(3):331.

C.11. At birth, what should be done to minimize an infant's risk of meconium aspiration syndrome?

In the past, obstetricians suctioned the mouth and nose of the newborn before the infant's first breath and the delivery of its shoulders. Currently, the American Heart Association and American Academy of Pediatrics as well as the ACOG recommend against this practice of routine oropharyngeal and nasopharyngeal suctioning in the presence of meconium-stained fluid based on the work by Vain et al. Similarly, experts also recommend that vigorous newborns with meconium exposure not be intubated and suctioned. Depressed newborns, however, should be intubated and be suctioned directly via the endotracheal tube to remove meconium from the airway. Exogenous surfactant administration to infants with meconium aspiration syndrome on ventilatory support has decreased the need for extracorporeal membrane oxygenation support.

American College of Obstetricians and Gynecologists. Management of delivery of a newborn with meconium-stained amnionic fluid. Committee Opinion No. 379, September 2007. American Heart Association and American Academy of Pediatrics. 2005 American Heart.

Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care of Pediatric and Neonatal Patients. Neonatal Resuscitation guidelines. *Pediatrics.* 2006;117(5):e1029–e1038.

Kliegman RM, Behrman RE, Jensen HB, et al., eds. *Nelson Textbook of Pediatrics.* 18th ed. Philadelphia: Saunders/Elsevier; 2007:742.

Vain NE, Szyld EG, Prudent LM, et al. Oropharyngeal and nasopharyngeal suctioning of meconium-stained neonates before delivery of their shoulders: multicentre, randomized controlled trial. *Lancet.* 2004;364:597.

C.12. The Apgar score of the newborn was 3 at 1 minute. How would you treat the newborn?

This newborn is depressed with the Apgar score of 3 and should have his trachea intubated followed by endotracheal suctioning. If ventilation with 100% oxygen does not lead to prompt improvement, umbilical vessel catheterization and appropriate fluid and drug administration is required.

American Heart Association and American Academy of Pediatrics. 2005 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care of Pediatric and Neonatal Patients: Neonatal Resuscitation guidelines. *Pediatrics* 2006;117(5):e1029–e1038.

C.13. Blood gases are sent immediately after delivery. What are the normal values for umbilical vein and artery blood gases?

Normally, umbilical artery blood has the following characteristics:

- pH value, 7.27 ± 0.069
- P_{CO_2}, 50.3 ± 11.1 mm Hg
- P_{O_2}, 22.0 ± 3.6 mm Hg
- Bicarbonate, 22.3 ± 2.5 mEq per L

Umbilical vein blood has the following characteristics:

- pH, 7.35 ± 0.05
- P_{CO_2}, 38.2 ± 5.6 mm Hg
- P_{O_2}, 29.2 ± 5.9 mm Hg
- Bicarbonate, 20.4 ± 2.1 mEq per L

Fetal conditions are reflected in the umbilical artery blood gas values, and umbilical vein blood gas determinations represent uteroplacental and maternal conditions. Ideally, both samples are collected. The ACOG recommends that cord blood gas measurements be performed when a cesarean section is done for fetal compromise or a low 5-minute Apgar score, severe growth restriction, abnormalities in FHR tracings, maternal thyroid disease, an intrapartum maternal fever, and/or multiple gestation exist(s). If any derangements exist, it is important to determine the metabolic versus respiratory contributions to the abnormalities. In 2003, the American Academy of Pediatrics and the ACOG defined metabolic acidosis as umbilical arterial pH <7.0 and a base deficit of at least 12 mmol/L; this acidosis may be considered a part of defining an acute intra-partum hypoxic episode that may be sufficient to cause cerebral palsy. Umbilical cord blood gas and pH measurements, however, are poorly predictive of immediate or long-term adverse neurologic outcome, but they do provide objective evidence of fetal metabolic state at birth.

American College of Obstetricians and Gynecologists. Umbilical cord blood gas and acid base analysis. Committee Opinion No. 348, November 2006.

American College of Obstetricians and Gynecologists and the American Academy of Pediatrics. Neonatal encephalopathy and cerebral palsy: defining the pathogenesis and pathophysiology. January 2003.

Bowe ET, Beard RW, Finster M, et al. Reliability of fetal blood sampling. Maternal fetal relationships. *Am J Obstet Gynecol.* 1970;107:279–287.

Cunningham FG, Leveno KJ, Bloom SL, et al., eds. *Williams Obstetrics.* 23rd ed. New York: McGraw-Hill; 2010:595–597.

Yeoman ER, Hauth JC, Gilstrap LC III, et al. Umbilical cord pH, P_{CO_2} and bicarbonate following uncomplicated term vaginal deliveries. *Am J Obstet Gynecol.* 1985;151:798.

D. Postoperative Management

D.1. Immediately after the baby was delivered, the patient's oxygen saturation decreased. What is the differential diagnosis?

The following may be likely causes of hypoxemia in this baby:

- Mechanical problems with the endotracheal tube
- Cardiac decompensation with pulmonary edema
- Pulmonary venous embolism: air, amniotic, thrombotic

Chestnut DH, Polley LS, Tsen LC, et al., eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Mosby/Elsevier; 2009:893.

Fong J, Gadalla R, Pierri MK, et al. Are Doppler-detected venous emboli during cesarean section air emboli? *Anesth Analg*. 1990;71:254.

CHAPTER 30

Appendectomy for a Pregnant Patient

FARIDA GADALLA

A 25-YEAR-OLD WOMAN

at 32 weeks' gestation presented to the emergency room with vague right sided abdominal pain. She had lost her appetite and had two episodes of vomiting. Temperature was 37.5° C (99.5° F), pulse rate, 100 beats per minute; hematocrit, 34%; and white blood cell count, 15,000/μL.

A. Medical Disease and Differential Diagnosis

1. What is the differential diagnosis for this patient?
2. How would you attempt to make the diagnosis of acute appendicitis clinically?
3. What is the incidence of appendicitis during pregnancy?
4. Is the incidence of gangrenous appendix higher in pregnant than in non-pregnant women? Why?
5. What is Alders sign?
6. What is the incidence of perforation of the appendix and in which trimester is it most likely to occur?
7. What is the incidence of surgery during pregnancy?
8. What are the main concerns associated with nonobstetric surgery in the pregnant patient?
9. What are the factors influencing teratogenicity in mammals? Discuss the teratogenicity of anesthetic agents.
10. Discuss the U.S. Food and Drug Administration (FDA) fetal risk categories for therapeutic agents and classify the most commonly used anesthetic agents.
11. How would you prevent intrauterine fetal asphyxia?
12. Although this patient presented with an acute abdomen, what is another reason for nonobstetric surgical intervention in the pregnant patient?

B. Preoperative Evaluation and Preparation

1. What would you discuss with this patient preoperatively?
2. Is there a difference in the aim of anesthesia for delivery and for nonobstetric surgery in a pregnant patient?
3. How would you premedicate this patient?

C. Intraoperative Management

1. What factors would alter your anesthetic technique from that used for a nonpregnant patient?
2. Describe your technique and dosage if you choose epidural anesthesia.
3. If the patient is in need of supplemental medication, what would be your choice?
4. What vasopressor would you choose to improve uteroplacental perfusion?
5. When this patient arrived in the operating room, she was panic-stricken and desired a general anesthetic. Describe your technique.
6. Does any controversy exist surrounding the use of nitrous oxide?
7. What is the incidence of fetal loss and what factors influence it?
8. If the patient were having surgery on her hand, what would you do differently?
9. What would you expect to see on the fetal monitor during a sevoflurane-nitrous oxide-oxygen anesthetic?
10. The surgeon schedules the procedure to be performed laparoscopically. Does this pose any problems?

D. Postoperative Management

1. When would you extubate this patient?
2. What monitors would you use postoperatively?
3. What other precautions would you take postoperatively?
4. What is the incidence of preterm delivery following nonobstetric surgery during pregnancy?
5. The next day, the patient went into premature labor having "failed" tocolytic therapy. She now needed a cesarean section for prematurity and breech presentation. She required another general anesthetic. In what way would your technique differ from your previous anesthetic technique?

A. Medical Disease and Differential Diagnosis

A.1. What is the differential diagnosis for this patient?

The differential diagnosis includes the following:

Medical conditions

- Sickle cell disease
- Porphyria
- Glomerulonephritis
- Pyelonephritis
- Pneumonia
- Withdrawal from drug addition

Obstetric conditions

- Labor
- Abruptio placentae
- Chorioamnionitis

Gynecologic conditions

- Salpingitis
- Degenerating myoma
- Ovarian cyst or tumor, either torted or ruptured
- Tubo-ovarian abscess

Surgical conditions

- Appendicitis
- Cholecystitis
- Pancreatitis
- Mesenteric adenitis
- Intestinal obstruction

Chestnut DH, Polley LS, Tsen LC, et al., eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Mosby; 2009:349.

A.2. How would you attempt to make the diagnosis of acute appendicitis clinically?

Diagnosis is based on a detailed history and the following symptoms:

- Vague abdominal pain, variable in position because of the growing uterus
- Anorexia
- Vomiting

The signs are the following:

- Abdominal tenderness
- Rebound pain
- Abdominal guarding
- Rectal tenderness
- Mildly elevated temperature, 37° C to 38° C (98.6° F to 100.4° F)
- Mildly elevated pulse rate
- An increase in white blood cell, although this is not useful because of the already existing relative leukocytosis in pregnancy

Chestnut DH, Polley LS, Tsen LC, et al., eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Mosby; 2009:349.

A.3. What is the incidence of appendicitis during pregnancy?

Appendicitis is the most common surgical emergency during pregnancy. The incidence varies from 1:350 to 1:10,000. Appendicitis is the reason for approximately 25% of operative indications for nonobstetric surgery during pregnancy. In epidemiologic studies, the reduced incidence of appendicitis in pregnant women compared to matched controls suggests a protective effect of pregnancy, especially in the third trimester.

Andersson REB, Lambe M. Incidence of appendicitis during pregnancy. *Internat J Epidemiol*. 2001;30(6):1281–1285.

Chestnut D. Polley LS, Tsen LC, et al., eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Mosby; 2009:349.

A.4. Is the incidence of gangrenous appendix higher in pregnant than in nonpregnant women? Why?

The incidence of gangrenous appendix has been reported to be higher during pregnancy because the enlarging uterus pushes the appendix away from the abdominal wall (Fig. 30.1), thereby causing the diseased appendix to produce little pain. This will delay the diagnosis and allow time for the appendix to become gangrenous. Recent studies using magnetic resonance imaging have confirmed that the appendix is displaced upward to a mean distance of 45 mm above the iliac crest at term. This will frequently result in flank pain instead of the typical right lower quadrant pain as the presenting symptom in some women. Another factor contributing to the delay in diagnosis of a nonobstetric abdominal crisis is that useful diagnostic procedures such as radiography and laparoscopy are postponed because of concern for the fetus.

Epidemiologic data, on the other hand, show no higher incidence of perforated appendix in pregnant women compared to matched controls.

Andersson REB, Lambe M. Incidence of appendicitis during pregnancy. *Internat J Epidemiol*. 2001;30(6):1281–1285.

Baden JM, Brodsky JB, eds. *The Pregnant Surgical Patient*. Mt. Kisco, NY: Futura Publishing; 1985:150.

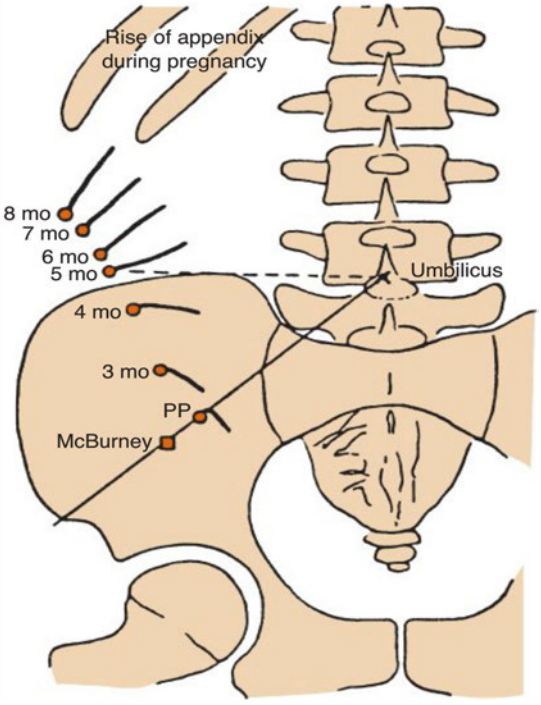

Figure 30.1 Changes in position and direction of the appendix during pregnancy. McBurney, McBurney's point; PP, prepregnancy. (Adapted from Baer JL, Reis RA, Arens RA. Appendicitis in pregnancy with changes in position and axis of normal appendix in pregnancy. *JAMA*. 1932;98:1359.)

Pates JA, Avendiano TC, Zaretsky MV, et al. The appendix in pregnancy: confirming historical observations with a contemporary modality. *J Reprod Med*. 2008;53:711–713.

Weingold AB. Appendicitis in pregnancy. *Clin Obstet Gynecol*. 1983;26:802.

Young BC, Hamar B, Levine D. Medical management of ruptured appendicitis in pregnancy. *Obstet Gynecol*. 2009;114(2):453–456.

A.5. What is Alders sign?

Alders sign is a clinical sign used to differentiate between uterine and appendiceal pain. The pain is localized with the patient supine. The patient then lies on her left side. If the area of pain shifts to the left, it is presumed to be uterine.

Alders N. A sign for differentiating uterine from extrauterine complications of pregnancy. *Br Med J*. 1951;2:1194.

A.6. What is the incidence of perforation of the appendix and in which trimester is it most likely to occur?

The incidence of perforation of the appendix is approximately 15%. Thirty percent of these occur in the first and second trimesters and 70% during the third trimester.

Chestnut DH, Polley LS, Tsen LC, et al., eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Mosby; 2009:337–357

Weingold AB. Appendicitis in pregnancy. *Clin Obstet Gynecol*. 1983;26:801.

A.7. What is the incidence of surgery during pregnancy?

The incidence of surgery is estimated at between 0.75% and 2.2%.

Baden JM, Brodsky JB, eds. *The Pregnant Surgical Patient*. Mt. Kisco, NY: Futura Publishing; 1985:223.

Mazze RI, Kallen B. Reproductive outcome after anesthesia and operations during pregnancy: a registry study of 5405 cases. *Am J Obstet Gynecol*. 1989;16:1178–1185.

Shnider SM, Webster GM. Maternal and fetal hazards of surgery during pregnancy. *Am J Obstet Gynecol*. 1965;92:891.

A.8. What are the main concerns associated with nonobstetric surgery in the pregnant patient?

The main concerns are maternal and fetal safety. To ensure maternal safety, awareness of the physiologic changes of the parturient is of great importance. Special care should be taken to prevent aspiration pneumonitis and supine hypotension syndrome. For fetal safety, it is essential to avoid teratogenic anesthetic agents and intrauterine fetal asphyxia.

Hawkins JL. Anesthesia for pregnant patient undergoing nonobstetric surgery. *ASA annual meeting refresher course lectures*. Park Ridge, IL: American Society of Anesthesiologists; 2006:430.

Rosen MA. Management of anesthesia for the pregnant surgical patient. *Anesthesiology*. 1999;91:1159–1163.

A.9. What are the factors influencing teratogenicity in mammals? Discuss the teratogenicity of anesthetic agents.

The factors influencing teratogenicity are genetic factors, nature, and dose of the anesthetic agent used, access of the agent to the fetus, and fetal developmental stage.

In this case, teratogenicity is unlikely because the most susceptible time in the human is that of organogenesis between the 15th and the 30th day after conception; susceptibility declines thereafter to the 50th day. Almost all anesthetics are teratogenic in some animals. Before implantation of the ovum, teratogenicity leads to abortion. Later, malformation, functional deficiencies, and even death can occur. Large retrospective studies in the United States and United Kingdom suggest that female anesthesiologists and the wives of male anesthesiologists had significantly increased incidence of spontaneous abortion, and their children were more likely to have congenital anomalies than those of nonoperating room physicians. It has been suggested that chronic exposure to trace anesthetic gases was the causative factor. However, no documented reports are found of teratogenicity in humans ascribed to any anesthetic agent used during pregnancy. Nevertheless, we recommend that only time-tested anesthetics, rather than new agents, be used for the pregnant patient, especially in the first trimester of pregnancy.

Cohen EN, Bellville WJ, Brown BW Jr. Anesthesia, pregnancy, and miscarriage: a study of operating room nurses and anesthetists. *Anesthesiology*. 1971;35:343.

Hawkins JL. Anesthesia for pregnant patient undergoing nonobstetric surgery. *ASA annual meeting refresher course lectures*. Park Ridge, IL: American Society of Anesthesiologists; 2006:430.

Rosen MA. Management of anesthesia for the pregnant surgical patient. *Anesthesiology*. 1999;91:1159–1163.

A.10. Discuss the U.S. Food and Drug Administration (FDA) fetal risk categories for therapeutic agents and classify the most commonly used anesthetic agents.

The FDA Fetal-risk Categories for Therapeutic Agents introduced in 1975 are the following:

- *Category A*: Controlled studies have shown no risk to the fetus during the first trimester and later trimesters as well. Risk is remote (e.g., water).
- *Category B*: Animal studies have demonstrated no fetal risk, but no controlled studies have been performed in humans. Animal studies have shown adverse fetal effects, but these results were not confirmed in controlled human studies. No risk is evident after the first trimester.
- *Category C*: Either studies have shown fetal risk in animals (teratogenic or embryocidal), but no controlled human studies have been performed, or there are no available data in humans or animals for an agent. Drugs of this class should be given only if the benefits outweigh the risks.
- *Category D*: Confirmed evidence exists for human fetal risk, but benefits are acceptable despite known risk (i.e., life or limb situations or serious disease for which no safer drugs exist [e.g., diazepam]).
- *Category X*: Agents of this class are contraindicated in pregnant patients for any reason because animal or human studies have displayed teratogenicity, or there is

evidence of fetal risk from prior human experience. Fetal risk clearly outweighs any clinical benefit of their use in pregnancy (e.g., thalidomide).

The commonly used anesthetic agents are classified as follows:

Induction agents

- Thiopental—C
- Methohexital—B
- Ketamine—C
- Etomidate—C
- Propofol—B

Inhalational agents

- Halothane—C
- Enflurane—B
- Isoflurane—B
- Desflurane—B
- Sevoflurane—B
- Nitrous oxide (no classification)

Local anesthetics

- 2-chloroprocaine—C
- Bupivacaine—C
- Lidocaine—B
- Ropivacaine—B

Narcotics

- Fentanyl—B
- Demerol—B
- Morphine—C
- Sufentanil—C

Although the FDA initially introduced categories in 1975, it has recently proposed a rule to eliminate the categories A, B, C, D, X for drug labeling and introduce a one-sentence advisory on drug labels to alleviate confusion among prescribers.

Food and Drug Administration. *Federal Register* 1980;44:37434–37436.

Food and Drug Administration. *Federal Register* 2008;73 no. 104/30831.

A.11. How would you prevent intrauterine fetal asphyxia?

It is essential to maintain maternal homeostasis to ensure fetal well-being. Fetal oxygenation is directly dependent on maternal oxygen tension, oxygen saturation, hemoglobin content, oxygen affinity, and uteroplacental perfusion. Maternal hypoxia will result in fetal hypoxia and, if uncorrected, fetal abnormalities or death. Factors that decrease uterine blood flow must be avoided. Uterine blood flow is determined by uterine vascular resistance and uterine perfusion pressure. Uterine blood flow may be decreased by the following: maternal hypotension, stress (which releases maternal catecholamines), pain, anxiety, hypoxia, hypercarbia, hyperventilation, positive pressure ventilation, and pressor agents.

The following principles govern the administration of anesthesia to parturients:

- Delay elective surgery until after delivery.
- Try to avoid surgery during the first trimester.

- Use regional anesthesia when feasible.
- Attach greater importance to anesthetic management than to agents used.
- Change anesthetic management to conform to changes in maternal physiology.

No anesthetic technique is truly precluded for surgery in the pregnant patient. The avoidance of maternal hypoxia, hypotension, and hypovolemia is of greater importance than the choice of anesthetic technique.

Chames MC, Peralman MD. Trauma during pregnancy: outcomes and clinical management. *Clin Obstet Gynecol*. 2008;51(2):398–408.

Hawkins JL. Anesthesia for pregnant patient undergoing nonobstetric surgery. *ASA annual meeting refresher course lectures*. Park Ridge, IL: American Society of Anesthesiologists; 2006:430.

Mhuireachtaigh RN, O'Gorman D. Anesthesia in pregnant patients for nonobstetric surgery. *J Clin Anesth*. 2006;18:60–66.

Rosen MA. Management of anesthesia for the pregnant surgical patient. *Anesthesiology*. 1999;91:1159–1163.

A.12. Although this patient presented with an acute abdomen, what is another reason for nonobstetric surgical intervention in the pregnant patient?

Trauma occurs in 5% to 10% of all pregnancies and ranks first among nonobstetric causes of maternal death. Trauma, particularly blunt trauma to the abdomen, can cause uterine rupture, mainly if the patient has had a previous cesarean surgery. Trauma is caused predominantly by traffic accidents and domestic violence.

American Congress of Obstetricians and Gynecologists. *Educational Bulletin No. 251*; September 1998.

National Safety Council. *Accident facts*. National Safety Council, 1987.

B. Preoperative Evaluation and Preparation

B.1. What would you discuss with this patient preoperatively?

It is important to discuss her options concerning regional versus general anesthesia, emphasizing that, statistically, the fetal outcome is similar, but regional anesthesia is the technique of choice for the mother.

Chestnut DH, Polley LS, Tsen LC, et al., eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Mosby; 2009:337–357.

Shelley WC. Anesthetic considerations for nonobstetric surgery. *Clin Perinatol*. 1982;9:149.

B.2. Is there a difference in the aim of anesthesia for delivery and for nonobstetric surgery in a pregnant patient?

Yes. The aim of obstetric anesthesia is to permit pain-free labor and delivery without interfering with the progress of labor, whereas the aim of surgical anesthesia is to provide maternal anesthesia without stimulating uterine activity and precipitating premature labor. Second, obstetric anesthesia should provide maternal analgesia

without fetal neurologic depression and delayed neonatal breathing. Surgical anesthesia, on the other hand, is designed to maintain uteroplacental perfusion but without consideration for fetal neurologic or respiratory depression.

Chestnut DH, Polley LS, Tsen LC, et al., eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia, PA: Mosby; 2009:337–357.

Diaz JH. Perioperative management of the pregnant patient undergoing non-obstetric surgery. *Anesth Rev*. 1991;18:21–27, 27–34.

B.3. How would you premedicate this patient?

Premedication may be avoided by reassurance and support. If necessary, barbiturates can be given for sedation. Glycopyrrolate, which does not cross the placental barrier, can be used as a vagolytic and antisialagogue.

A nonparticulate antacid, such as 30 mL of 0.3 M sodium citrate, given about 30 minutes before surgery to prevent aspiration pneumonitis, and an H_2 receptor antagonist may also be given.

Chestnut DH, Polley LS, Tsen LC, et al., eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Mosby; 2009:353.

Shelley WC. Anesthetic considerations for non-obstetric surgery. *Clin Perinatol*. 1982;9:149.

C. Intraoperative Management

C.1. What factors would alter your anesthetic technique from that used for a nonpregnant patient?

The anatomic and physiologic changes of pregnancy alter the anesthetic technique in the following systems:

Cardiovascular system

- Increased blood volume (more increase in plasma than in red blood cell count)
- Increased cardiac output (stroke volume and heart rate)
- Decreased peripheral resistance
- Decreased mean arterial blood pressure
- Vena caval and aortic compression in the supine position as shown in Figure 30.2. Therefore, the pregnant patient should be tilted by a wedge under her right hip.

Respiratory system

- Increased minute ventilation
- Increased oxygen consumption
- Decreased functional residual capacity as shown in Figure 30.3

Gastrointestinal system

- Decreased gastrointestinal motility and increased gastric emptying time
- Decreased volume of gastrointestinal secretions
- Increased gastric acidity
- Decreased lower esophageal tone because of increased progesterone level. For these reasons, a pregnant patient beyond the first trimester should always be considered as having a full stomach and must be considered at risk for regurgitation and aspiration

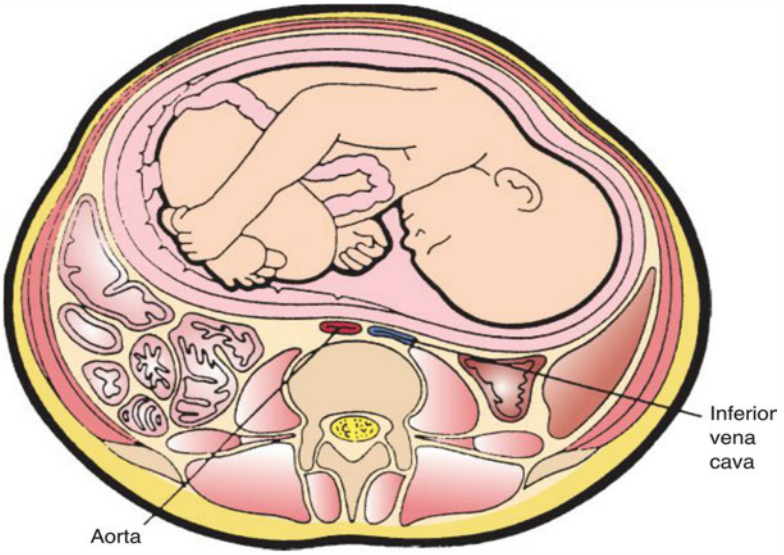

Figure 30.2 The pregnant uterus compressing the aorta and the inferior vena cava (aortocaval compression) in supine position. (Adapted from Ostheimer GW. *Regional Anesthesia Techniques in Obstetrics*. New York: Breon Laboratories; 1980.)

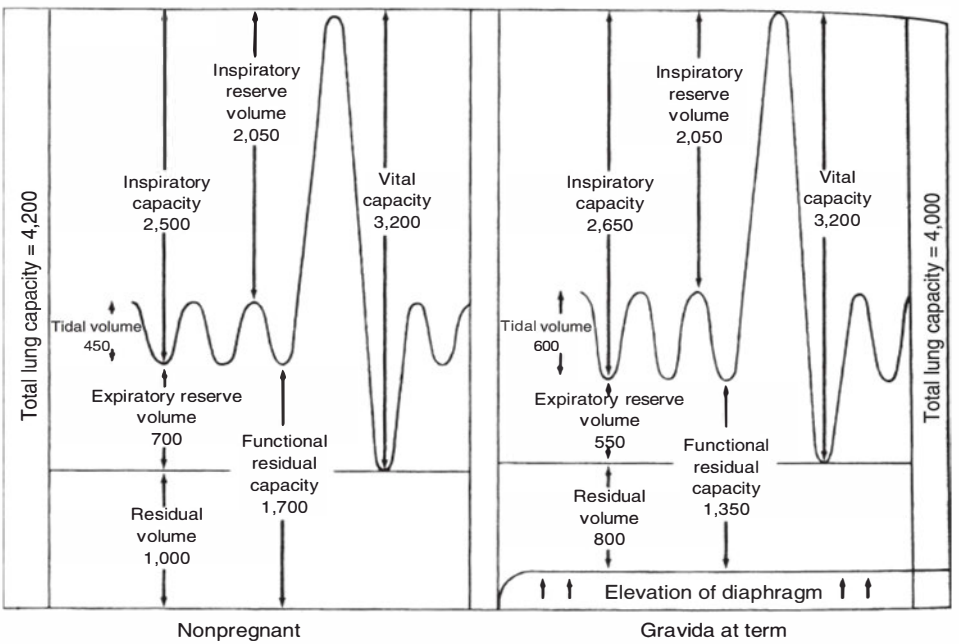

Figure 30.3 Pulmonary volumes and capacities during pregnancy. (From Bonica JJ. *Principles and Practice of Obstetric Analgesia and Anesthesia*. Philadelphia: FA Davis Co; 1967, with permission.)

Central nervous system

- Decreased minimal alveolar concentration (MAC) of inhaled anesthetics
- Increased sensitivity to local anesthesia
- Decreased volume of epidural anesthetic required, because of engorgement of epidural veins and consequent decrease in size of epidural space

Skin and mucous membranes

- More friable mucous membranes and engorged mucosal capillaries (Therefore, avoid insertion of nasal airways, nasotracheal, and nasogastric tubes.)

Metabolic

- Increase in oxygen consumption by 20%

Chestnut DH, Polley LS, Tsen LC, et al., eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Mosby; 2009:15–36.

C.2. Describe your technique and dosage if you choose epidural anesthesia.

The patient is placed on her side or in the sitting position for epidural placement. Adequate hydration is achieved with intravenous fluids. The epidural block is placed at L2–3 or L3–4 using the loss-of-resistance or hanging-drop technique. After testing for inadvertent spinal or intravascular placement, the local anesthetic is given in divided doses to attain a T4 level. This takes between one-half and two-thirds of the dose used for a nonpregnant patient (between 18- and 24-mL average volume). An inadvertent spinal injection is detected by the rapid onset of a solid motor block following a 2- to 5-mL test dose; and an intravascular injection is evidenced by signs of systemic toxicity (e.g., dizziness, tinnitus, circumoral numbness).

The patient is once again placed in the left lateral decubitus position, oxygen is delivered by nasal cannula, and her blood pressure is monitored closely.

The choices of local anesthetics are either 2% lidocaine or 0.5% bupivacaine. These agents afford good analgesia with a degree of motor blockade that provides muscular relaxation. The addition of epidural fentanyl promotes a quicker onset and more solid block.

Chestnut DH, Polley LS, Tsen LC, et al., eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Mosby; 2009:233–235.

Hughes SC, Levinson G, Rosen MA, eds. *Shnider and Levinson's Anesthesia for Obstetrics*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2002:2249.

C.3. If the patient is in need of supplemental medication, what would be your choice?

It is best to use the narcotics that have been tried by time and appear to be safe, such as morphine and fentanyl. Small doses of ketamine (0.25 mg/kg intravenously) may also be given.

Chestnut DH, Polley LS, Tsen LC, et al., eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Mosby, 2009:353.

Hughes SC, Levinson G, Rosen MA, eds. *Shnider and Levinson's Anesthesia for Obstetrics*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2002:249.

C.4. What vasopressor would you choose to improve uteroplacental perfusion?

Ephedrine was considered the safest vasopressor because it increases mean arterial pressure and uterine artery blood flow without a concomitant decrease in uteroplacental perfusion. The overall increase in cardiac output from the β-adrenergic stimulation of ephedrine will maintain uterine artery perfusion and compensate for its mild adrenergic vasoconstriction. Currently, the ban on pure alpha agonists has been lifted because a number of current studies involving the use of both ephedrine and phenylephrine to treat maternal hypotension during spinal anesthesia for cesarean section show that phenylephrine does not adversely affect neonatal outcome and decreases the incidence of fetal acidosis.

Chestnut DH, Polley LS, Tsen LC, et al., eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Mosby; 2009:347.

Diaz JH. Perioperative management of the pregnant patient undergoing non-obstetric surgery. *Anesth Rev*. 1991;18:21–27, 27–34.

Lee A, Ngan Kee WD, Gin T. A quantitative, systematic review of randomized controlled trials of ephedrine versus phenylephrine for the management of hypotension during spinal anesthesia for cesarean delivery. *Anesth Analg*. 2002;94(4):920–926.

Ngan Kee WD, Khaw KS, Tan PE, et al. Placental transfer and fetal metabolic effects of phenylephrine and ephedrine during spinal anesthesia for cesarean delivery. *Anesthesiology*. 2009;111(3):506–512.

C.5. When this patient arrived in the operating room, she was panic-stricken and desired a general anesthetic. Describe your technique.

- Check the adequacy of the intravenous.
- Preoxygenate for at least 3 minutes to ensure denitrogenation in the lungs and to avoid maternal and fetal hypoxemia during induction and intubation.
- Carry out induction using a rapid-sequence technique (thiopental sodium or propofol, succinylcholine, and intubation using a cuffed endotracheal tube with a 7-mm internal diameter or less).
- Carry out maintenance using agents with a long history of safety, including morphine, fentanyl, succinylcholine, nondepolarizing muscle relaxants, sevoflurane, desflurane, and nitrous oxide-to-oxygen 50:50. The inhalation anesthetics have the added advantage of relaxing the uterus in the hope of preventing premature labor. Air/oxygen can also be used with the understanding that the omission of nitrous oxide can result in a drop in maternal blood pressure because of the need to use a higher concentration of volatile agents.
- Avoid hyperventilation and hypoventilation.
- Extubate when the patient is awake and has regained laryngeal reflexes.

Chestnut DH, Polley LS, Tsen LC, et al., eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Mosby; 2009:353.

C.6. Does any controversy exist surrounding the use of nitrous oxide?

Yes, especially during early pregnancy. This is because nitrous oxide inhibits methionine synthetase, potentially affecting DNA synthesis.

Nitrous oxide also increases adrenergic tone and decreases uterine blood flow. This, however, can be prevented by the addition of a volatile agent.

Nitrous oxide can cause teratogenic effects in animals during prolonged exposure at critical times. However, teratogenicity has not been demonstrated in humans.

Chestnut DH, Polley LS, Tsen LC, et al., eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Mosby; 2009:347.

Hawkins JL. Anesthesia for the pregnant patient undergoing nonobstetric surgery. *ASA refresher courses in anesthesiology*, Vol. 25. Park Ridge, IL: American Society of Anesthesiologists; 1997:100–105.

Rosen MA. Management of anesthesia for the pregnant surgical patient. *Anesthesiology*. 1999;91:1159–1163.

C.7. What is the incidence of fetal loss and what factors influence it?

Prenatal loss may be caused by premature labor, but it can also be caused by generalized peritonitis and sepsis. Fetal loss is related more to the severity of the disease than to the surgical procedure or the anesthetic. The perinatal mortality rate in cases of prematurity because of generalized peritonitis is 200 to 350 per 1,000. The perinatal mortality rate for nonperforated appendicitis is approximately 50 per 1,000 women.

Chestnut DH, Polley LS, Tsen LC, et al., eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Mosby; 2009:349.

Duncan PG, Pope WDB, Cohen MM, et al. Fetal risk of anesthesia and surgery during pregnancy. *Anesthesiology*. 1986;64:790–794.

Shnider SM, Webster GM. Maternal and fetal hazards of surgery during pregnancy. *Am J Obstet Gynecol*. 1965;92:891.

Weingold AB. Appendicitis in pregnancy. *Clin Obstet Gynecol*. 1983;26:801.

C.8. If the patient were having surgery on her hand, what would you do differently?

Initially, offer the patient the choice of a brachial plexus block or an intravenous regional technique. It is possible to monitor the fetal heart during surgery and to monitor for uterine contractions using a tocodynamometer. Continuous fetal heart monitoring using transabdominal doppler is possible at approximately 18 weeks' gestation.

Biehl DR. Foetal monitoring during surgery unrelated to pregnancy. *Can Anaesth Soc J*. 1985;32:455–459.

Hughes SC, Levinson G, Rosen MA, eds. *Shnider and Levinson's Anesthesia for Obstetrics*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2002:249.

C.9. What would you expect to see on the fetal monitor during a sevoflurane-nitrous oxide-oxygen anesthetic?

One would expect to see a decrease in beat-to-beat variability during anesthesia using inhalation agents.

Chestnut DH, Polley LS, Tsen LC, et al., eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Mosby; 2009:352.

Liu PL. Clinical reports: fetal monitoring in patients undergoing surgery unrelated to pregnancy. *Can Anaesth Soc J*. 1985;32:525–532.

C.10. The surgeon schedules the procedure to be performed laparoscopically. Does this pose any problems?

Laparoscopy has been performed during pregnancy both for diagnostic and procedural surgery. CO_2 pneumoperitoneum can cause fetal respiratory acidosis. This leads to the recommendation of maintaining low intra-abdominal pressure, limiting the duration of surgery, and using arterial blood gas analysis. However, a recent study concluded that capnography is adequate to guide ventilation during laparoscopic surgery. End-tidal CO_2 should be maintained at approximately 32 mm Hg. Fetal outcomes were similar in patients undergoing laparoscopy versus laparotomy in pregnancies between 4 and 20 weeks of surgery.

Bhavani-Shankar K, Steinbrook RA, Brooks DC, et al. Arterial to end-tidal carbon dioxide pressure difference during laparoscopic surgery in pregnancy. *Anesthesiology*. 2000;93:370–373.

Hawkins JL. Anesthesia for pregnant patient undergoing nonobstetric surgery. *ASA annual meeting refresher course lectures*. Park Ridge, IL: American Society of Anesthesiologists; 2006:430.

Reedy MB, Kallen B, Kuehl TJ. Laparoscopy during pregnancy: a study of five fetal outcome parameters with use of the Swedish Health Registry. *Am J. Ob Gyn*. 1997;177(3):673–679..

D. Postoperative Management

D.1. When would you extubate this patient?

The patient can be extubated when she is fully awake, in command of her airway reflexes and able to avoid pulmonary aspiration.

Chestnut DH, Polley LS, Tsen LC, et al., eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Mosby; 2009:353.

Hughes SC, Levinson G, Rosen MA, eds. *Shnider and Levinson's Anesthesia for Obstetrics*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2002:249.

D.2. What monitors would you use postoperatively?

- Electrocardiogram
- Pulse oximeter
- Urinary catheter (to be discontinued within 24 hours, unless specifically indicated)
- Intermittent blood pressure and temperature monitoring
- Tocodynamometer to detect premature labor
- Fetal heart monitor to ensure fetal well-being

Chestnut DH, Polley LS, Tsen LC, et al., eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Mosby; 2009:353.

Shnider SM, Levinson G, eds. *Anesthesia for Obstetrics*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2002:262.

D.3. What other precautions would you take postoperatively?

- Provide adequate hydration.
- Continue left uterine displacement.
- Administer supplemental oxygen.

Many obstetricians use heavy sedation plus a course of β-agonist drugs to prevent premature labor. It is recommended that pregnant patients should be observed on the obstetric floor for a minimum of 12 hours following nonobstetric surgery. Magnesium sulfate is given intravenously if labor occurs.

Chestnut DH, Polley LS, Tsen LC, et al., eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Mosby; 2009:354.

Hughes SC, Levinson G, Rosen MA, eds. *Shnider and Levinson's Anesthesia for Obstetrics*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2002:249.

D.4. What is the incidence of preterm delivery following nonobstetric surgery during pregnancy?

In a study of 778 women who underwent appendectomy while pregnant, 22% delivered during the following week if surgery occurred between 24 and 36 weeks' gestation.

Mazza RI, Källen B. Appendectomy during pregnancy. A Swedish registry study of 778 cases. *Obstet Gynecol*. 1991;77:835–840.

D.5. The next day, the patient went into premature labor having "failed" tocolytic therapy. She now needed a cesarean section for prematurity and breech presentation. She required another general anesthetic. In what way would your technique differ from your previous anesthetic technique?

- Do not administer a defasciculating dose of nondepolarizing muscle relaxants prior to administration of succinylcholine. Magnesium sulfate prevents the muscle fasciculations that normally occur following the administration of succinylcholine.
- Use smaller doses of muscle relaxants since magnesium sulfate potentiates their effects.
- Avoid the use of narcotics until after delivery, then stop the inhalation agent and begin using a narcotic technique.

Chestnut DH, Polley LS, Tsen LC, et al., eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 4th ed. Philadelphia: Mosby; 2009:544, 763.

Hughes SC, Levinson G, Rosen MA, eds. *Shnider and Levinson's Anesthesia for Obstetrics*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2002:249.

SECTION VIII

The Hematologic System

CHAPTER 31

Hemophilia and Coagulation Disorders

Jonathan Leff, Linda Shore-Lesserson, and Robert E. Kelly

A 46-YEAR-OLD MAN

with hemophilia and HIV-positive status was scheduled for elective elbow synovectomy with resection of the radial head because of limited, painful range of motion.

A. Medical Disease and Differential Diagnosis

1. What are the differences between hemophilia A, B, and C?
2. Describe the typical history and pathophysiology associated with von Willebrand disease (vWD).
3. What are the different components of factor VIII?
4. What is the difference between platelet adhesion and platelet aggregation?
5. Describe the physiologic events that occur following endothelial interruption in the blood vessel.
6. What prevents the extension of a clot beyond the site of injury?
7. Describe the procoagulant factors involved in the extrinsic, intrinsic, and common coagulation cascade.
8. Describe the levels of factor VIII necessary for hemostasis.
9. Describe the various laboratory tests that evaluate the coagulation cascade and the specific components measured by each.
10. Would there be any differences in preoperative factor replacement therapy between a patient with hemophilia A or hemophilia B?

B. Preoperative Evaluation and Preparation

1. What steps would you take to correct this patient's coagulation status before surgery?
2. What is meant by 1 unit of factor VIII clotting activity and how much does 1 unit of factor VIII clotting activity per kilogram of body weight increase factor VIII concentrations?
3. Would you administer factor VIII using a bolus or infusion technique?
4. Can a hemophiliac patient fail to mount an appropriate coagulation response following factor VIII infusion?
5. If a patient with hemophilia does not respond to a bolus injection of factor VIII, can an infusion technique be effective?
6. How much factor VIII activity is present in fresh frozen plasma (FFP)? What are the risks associated with administration of FFP?
7. What are the indications for the administration of FFP?
8. How is cryoprecipitate prepared? What are the components in cryoprecipitate? How much factor VIII activity is present in cryoprecipitate? What are the indications for cryoprecipitate?
9. Describe the advantages and disadvantages of the products that are available for transfusion of factor VIII activity.
10. What is the role of desmopressin D-arginine vasopressin (DDAVP) for hemostatic management in this patient?
11. What is the role of ε-aminocaproic acid (EACA) in the perioperative period for the patient with hemophilia?
12. Is there a role for recombinant activated factor VII (rFVIIa) in the treatment of hemophilia?
13. What is the mechanism and dosing of rFVIIa?

C. Intraoperative Management

1. Is it safe to administer an intramuscular injection to this patient before surgery?
2. Would an axillary block be appropriate for this patient?
3. If general anesthesia is used as a technique, would it be safe to intubate the patient's trachea?
4. Would you use any special precautions for this patient who is positive for HIV?
5. What special considerations should be taken in choosing anesthetic drugs for this patient?
6. During the operative procedure, the surgeon indicated that significant blood loss had occurred. Would you transfuse this patient with packed red blood cells or whole blood?
7. During the transfusion of the first unit of whole blood, the patient's temperature rose from 36.8° C to 37.9° C (98.24° F to 100.22° F). What immediate steps should be taken by the anesthesiologist at this time?
8. Does giving blood intraoperatively increase the potential for the development of factor VIII inhibitors?
9. Can factor VIII be safely administered to patients who have developed circulating inhibitors?
10. The surgeon has requested the use of a tourniquet to minimize surgical bleeding. What are the physiologic and hemodynamic responses to tourniquet use?
11. Is it appropriate to suction the endotracheal tube and oropharynx of this patient before extubation?

D. Postoperative Management

1. What special consideration should be given to postoperative pain management for this patient?
2. What steps should be taken to enhance the coagulation status of this patient in the postoperative period while at home?
3. Can this patient be treated with factor VIII supplements using home infusion?

A. Medical Disease and Differential Diagnosis

A.1. What are the differences between hemophilia A, B, and C?

Hemophilia, one of the oldest known genetic disorders, can be classified into type A, B, or C. Hemophilia A (factor VIII deficiency) is the most common form, accounting for 85% of all patients with hemophilia. The World Federation of Hemophilia estimates 315,000 individuals in the world are afflicted with hemophilia A. It is an X-linked recessive disorder, and therefore occurs in men and homozygous women. Approximately 30% of patients have no family history of this disease; presumably their disease is caused by a new mutation. The disease results in a hemorrhagic tendency that, in its most severe form, can be life threatening. A screening test for hemophilia A is the partial thromboplastin time (PTT), which will be prolonged in all patients except those with mild disease. Measuring factor VIII activity will provide a definitive diagnosis.

Patients with hemophilia B present with either deficient or defective factor IX; this entity represents 14% of hemophilia patients. This X-linked genetic disorder has an inheritance pattern and clinical features that are similar to those of hemophilia A, but can be diagnosed by measuring both the concentration and function of factor IX.

The remaining 1% of hemophiliac patients suffer a deficiency in factor XI and is classified as hemophilia C, an autosomal disorder that is extremely rare except in Ashkenazi Jews. Hemophilia C can be distinguished from A and B by the absence of bleeding into joints and muscles. In addition, the degree of factor XI deficiency may not predict a patient's bleeding tendency in the postoperative period.

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:397–400.

Behrman RE, Kleigman RM, Jenson HB, et al., eds. *Nelson Textbook of Pediatrics*. 18th ed. Philadelphia: WB Saunders; 2007:1508–1511.

Perkins JT, Vender JS. Transfusion therapy. In: Collins VJ, ed. *Physiologic and Pharmacologic Bases of Anesthesia*. Baltimore: Williams & Wilkins; 1996:221.

Prasad M, Ted R. *Hemophilia C*. Montoya Hemophilia Center, Department of Pediatrics, University of New Mexico. May 15, 2006.

Hines RL, Marschall KE, eds. Stoelting's *Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone; 2008:420.

A.2. Describe the typical history and pathophysiology associated with von Willebrand disease (vWD).

vWD is the most common congenital bleeding disorder. The most common form of the disease is inherited as an autosomal dominant trait and has an incidence cited as high as 2% to 3%. Patients with vWD have a prolonged bleeding time, which clinically manifests as bruising, epistaxis, mucocutaneous bleeding, and menorrhagia in women. The diagnosis is suggested by the patient's history of a bleeding diathesis and the presence of a prolonged bleeding time, despite a normal platelet count. Laboratory analysis of vWD is useful for classifying the subtypes and to guide therapy. Type I vWD represents most afflicted patients and is marked by decreased levels of normal von Willebrand factor (vWF). First-

line treatment in type I disease is with desmopressin (L-deamino-8-D-arginine-vasopressin [DDAVP]). Cryoprecipitate and FFP also contain vWF and may be used in patients unresponsive to DDAVP. Type IIA vWD represents 15% to 30% of patients and is a qualitative defect in the platelet–vWF interaction. The number of vWF proteins can be normal, but there is an absence of high and middle molecular weight vWF multimers. Type IIB vWD represents that subset of patients with enhanced platelet aggregation in the presence of ristocetin. Ristocetin is an antibiotic formerly used to treat staphylococcus infection, which also initiates binding of vWF to platelet glycoprotein IB. In the absence of vWF, no agglutination will occur with the ristocetin cofactor activity assay. A second assay was developed, termed the *ristocetin-induced platelet agglutination*, which uses the patient's own platelets and plasma. This test is useful to distinguish a hyperaggregation tendency such as observed in type IIB vWD. In type IIN (Normandy) there is a decreased affinity of vWF, to factor VIII, and these patients are often misdiagnosed as having hemophilia A. The response to plasma can be helpful in distinguishing vWF deficiency from hemophilia. Hemophilia A patients will have a rapid rise of factor VIII levels following plasma or cryoprecipitate infusion, but this is not sustained. The patients with vWD experience a similar initial rise in factor VIII; in contrast to hemophilia A, these patients are able to sustain the increase for over 48 hours. Types I and II vWD are inherited as autosomal dominant. Patients with type III vWF deficiency have little or no vWF multimers. DDAVP is not of benefit because these patients have no endogenous production of vWF. Type III vWD is inherited as an autosomal recessive trait. Types IIB and III are extremely rare. It is important to distinguish the subtypes of vWD because the use of DDAVP in types IIB and III may cause thrombocytopenia and increase platelet agglutination.

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins, 2009:397–398.

Behrman RE, Kleigman RM, Jenson HB, et al., eds. *Nelson Textbook of Pediatrics*. 18th ed. Philadelphia: WB Saunders, 2007:1508–1511.

Prasad M, Ted R. *Hemophilia C*. Montoya Hemophilia Center, Department of Pediatrics, University of New Mexico. May 15, 2006.

Hines RL, Marschall KE, eds. Stoelting's *Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone, 2008:419–420.

Hines RL, Marschall KE, eds. Stoelting's *Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone; 2008:427–429

A.3. What are the different components of factor VIII?

Coagulant factor VIII is a plasma protein that has two components, factor VIII vWF and vWF VIII:c, each of which is under separate genetic control. The von Willebrand's component serves to adhere platelets to collagen in the subendothelial layer of blood vessels during primary hemostasis and to carry the factor VIII molecule. In hemophilia A, this factor VIII is deficient in quantity or quality.

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins, 2009:389.

A.4. What is the difference between platelet adhesion and platelet aggregation?

Platelet adhesion is the affinity of platelets for nonplatelet surfaces, whereas platelet aggregation is the affinity of platelets for each other.

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins, 2009:388.

A.5. Describe the physiologic events that occur following endothelial interruption in the blood vessel.

The small size of platelets relative to other blood components, such as red or white cells, results in slower transit in the blood vessel with resultant margination, the process in which the faster moving larger components push the platelets toward the walls of the blood vessel. As a result, platelets are in contact with the surface of the blood vessel and can immediately detect any break in the endothelium. Any endothelial break exposes platelets to subendothelial structures, including collagens and other activating proteins, which cause the glycoprotein receptors on the platelets to rapidly adhere to these substances. This adhesion begins the process of platelet activation, in which the shape of the platelet is changed and the contents of the cytoplasmic granule are released. These substances include factors such as adenosine diphosphate (ADP), which further stimulate platelet aggregation. The platelet plug that is formed in this process provides initial hemostasis; interaction with both fibrin and thrombin fuse the platelet plug for continued hemostasis. Activation of factor XIII produces cross-polymerization of the loose fibrin to produce a firm clot.

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins, 2009:387–389.

Hines RL, Marschall KE, eds. Stoelting's *Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone, 2008:417–418.

A.6. What prevents the extension of a clot beyond the site of injury?

Localization of coagulation and control of primary hemostasis are controlled by many factors, including the dynamic tension between two prostaglandins, thromboxane A_2 and prostacyclin. Thromboxane A_2 is released at the site of vascular injury and stimulates vasoconstriction, ADP release, and platelet aggregation. In contrast, prostacyclin is produced by intact endothelial cells and prevents platelet aggregation and clot formation. In addition, clot localization is maintained by the dilution of procoagulants in the blood, the removal of activated factors by the liver, the action of circulating procoagulant inhibitors such as antithrombin III and protein C, and the release of the serene protease tissue plasminogen activator. The tissue plasminogen activator digests fibrinogen as well as factors V and VIII, initiating the physiologic process of fibrinolysis and resulting in fibrin degradation (split) products, which are removed by the mononuclear phagocyte system.

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins, 2009:390–391.

Hines RL, Marschall KE, eds. Stoelting's *Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone; 2008:417–422

A.7. Describe the procoagulant factors involved in the extrinsic, intrinsic, and common coagulation cascade.

When normal blood is placed in a test tube, a clot will form without any added agents. The clotting factors involved in this reaction were originally classified as the "intrinsic" factors, because everything necessary for blood to clot was "intrinsic" to the test tube. The "extrinsic" path is another potent stimulus for thrombin formation and is initiated by exposure of tissue thromboplastin (tissue factor) to factor VII. The extrinsic and intrinsic pathways converge at factor X to form the common pathway.

This classic separation of procoagulant factors into extrinsic, intrinsic, and common coagulation cascades is not absolute because of the crossover of many factors. In fact, the current conception of coagulation uses a cell-based model and

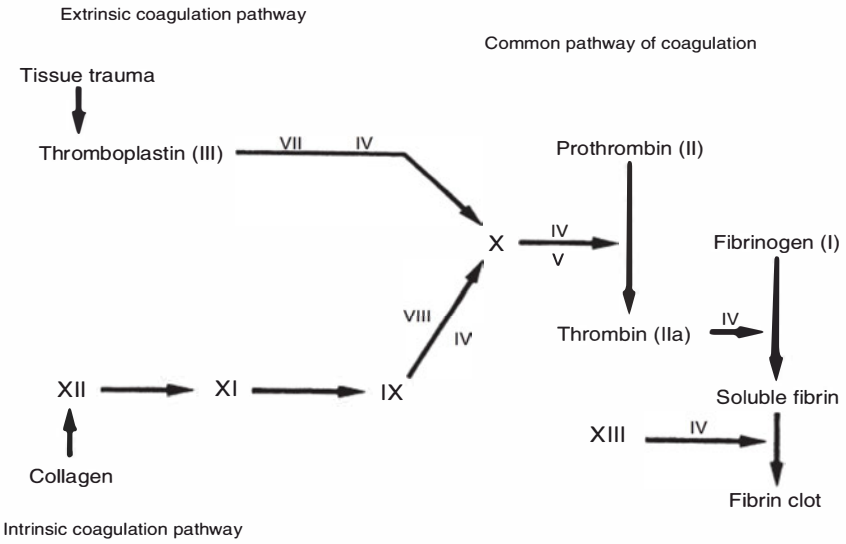

Figure 31.1 Schematic diagram of the procoagulant phase of coagulation depicting the cascade sequence in three steps, designated as the intrinsic, extrinsic, and common coagulation pathways. (From Stoelting RK, Dierdorf SF, McCammon RL, eds. *Anesthesia and Co-existing Disease*. 2nd ed. New York: Churchill Livingstone; 1988:577, with permission.)

takes into account many in vivo pathways and the contribution of the endothelium itself. Although the classic intrinsic and extrinsic coagulation pathways does lead to the formation and activation of thrombin (and hence the amplification of coagulation), it fails to take into account the cellular components, which play a vital role in hemostasis.

The cell-based theory is thought to occur in three stages: initiation, amplification, and propagation. Each stage represents a different aspect of hemostasis at a cellular level, with the end result being formation of thrombin and a stable clot. An appreciation of thrombin's role in the coagulation cascade is critical, and the coagulation cascade is the reason that all anticoagulation therapy is aimed at the inhibition of thrombin. In fact, the initiation phase of the cell-based model is marked by the exposure of tissue factor to circulating factor VII. This activates the other two phases and serves as a potent catalyst for hemostasis. An understanding of this mechanism helps to illustrate how the drug Novoseven (activated factor VII) is such an effective hemostatic agent. The common coagulation cascade is shown in Figure 31.1.

Hoffman M, Monroe DM III. A cell-based model of hemostasis. *Thromb Haemost*. 2001;85:958–965.

Hines RL, Marschall KE, eds. Stoelting's *Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone; 2008:417–419

A.8. Describe the levels of factor VIII necessary for hemostasis.

The levels of factor VIII necessary for hemostasis are described in Table 31.1. When life-threatening airway or neurologic bleeding has occurred, factor VIII levels of 100% should be achieved. Similarly, when major surgery is anticipated, correction to 100% factor VIII levels should be done preoperatively and maintained postoperatively (see section D.2).

Table 31.1 Levels of Factor VIII Necessary for Hemostasis

CLINICAL PRESENTATION	FACTOR VIII CONCENTRATION (% OF NORMAL)
Spontaneous hemorrhage	1–3
Moderate trauma	4–8
Hemarthrosis and deep skeletal muscle hemorrhage	10–15
Major surgery	> 30

Jamco RL, McClean WE, Terrin JM, et al. A prospective study of patterns of bleeding in boys with hemophilia. *Haemophilia.* 1996;2:202–206.

Maxwell LB, Zuckerberg AL, Motoyama EK, et al. Systemic disorders in pediatric anesthesia. In: Motoyama EK, Davis PJ, eds. *Smith's Anesthesia for Infants and Children*. St. Louis: Mosby; 1996:857.

Hines RL, Marschall KE, eds. Stoelting's *Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone; 2008:419–420

A.9. Describe the various laboratory tests that evaluate the coagulation cascade and the specific components measured by each.

Numerous laboratory tests evaluate specific components of the coagulation cascade. The standard skin bleeding time is one way to measure for platelet function, although bleeding time may be prolonged as a result of factors other than platelet dysfunction such as anemia, low platelet count, or patient movement. Moreover, no study has reported a correlation between an abnormal bleeding time and an increased risk for hemorrhage. More recent tests for analyzing platelet function include the VerifyNow and the platelet function analyzer (PFA-100). VerifyNow (Accumetrics, San Diego, CA), a point-of-care monitor designed specifically to measure the platelet response to a thrombin receptor agonist peptide. In whole blood, it measures thrombin receptor agonist peptide activation-induced platelet agglutination of fibrinogen-coated beads using an optical detection system. Because of the importance of the GPIIb IIIa receptor in mediating fibrinogen–platelet interactions, the Ultegra has been especially useful in accurately measuring receptor inhibition in patients undergoing invasive cardiologic therapy receiving GPIIb IIIa–inhibiting drugs. The platelet function analyzer, PFA-100 (Dade Behring, Miami, FL), is a monitor of platelet adhesive capacity that is valuable in its diagnostic abilities to identify drug-induced platelet abnormalities, Bernard-Soulier syndrome, 9vWD, and other acquired and congenital platelet defects. The test is conducted as a modified in vitro bleeding time. Whole blood is drawn through a chamber by vacuum and is perfused across an aperture in a collagen membrane–coated with an agonist (epinephrine or ADP). Platelet adhesion and formation of aggregates will seal the aperture, thereby indicating the "closure time" measured by the PFA-100. This test may be useful in detecting pharmacologic platelet dysfunction before cardiac surgery or may be able to accurately detect hypercoagulability after cardiopulmonary bypass.

Monitoring the coagulation cascade is usually performed with both prothrombin time (PT) and PTT. The PT is measured by adding tissue form thromboplastin (TF) to a blood specimen and measuring the time until clot formation. This test will detect abnormalities in factors I, II, V, VII, or X. A normal PT could occur with an abnormal

fibrinogen level because PT is only prolonged if the fibrinogen level is below 100 mg per day. In order to homogenize test results performed with different types of thromboplastin activating agents, standardization to the international sensitivity index has created the international normalized ratio (INR). The PTT is obtained when partial thromboplastin is added to a test tube of blood and time is measured until clot forms, measuring factors I, II, V, VIII, IX, X, XI, and XII. This test can be modified by the addition of the surface activating factors XI and XII before the addition of the partial thromboplastin, creating the activated partial thromboplastin time (APTT). The APTT is a faster test than the PTT and is a standard test used in clinical practice. The activated clotting time also is an accelerated version of the PTT and is activated by diatomaceous earth. This test is used most often to measure the efficiency of heparin use and is much less sensitive than the APTT to specific factor deficiencies. The thrombin time bypasses most of the coagulation cascade to measure the conversion of fibrinogen to fibrin, a useful test to determine both inadequate amounts of fibrinogen as well as inadequate fibrinogen molecules. The thromboelastogram (TEG) measures speed of clot formation and clot firmness. This monitor allows evaluation of a clot from early fibrin strand to fibrinolysis. The TEG tracing is made up of several parameters; reaction time (R value), coagulation time (K value), maximum amplitude (MA value), an α angle, and the amplitude 60 degrees after the MA (A60). A deviation from a prototypical tracing represents a specific abnormality in the patient's coagulation cascade. An abnormal TEG tracing can correspond to conditions such as thrombocytopenia or factor deficiencies, allowing systematic analysis of intraoperative coagulation defects and a more directed approach to therapy (see Chapter 13, section A.22).

Laboratory evaluation of the coagulation cascade can be defined as shown in Table 31.1.

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins, 2009:392–396.

Fischer GW, Shore-Lesserson L. Hematologic diseases. In: Fleisher L, ed. *Anesthesia and Uncommon Diseases*. 5th ed. Philadelphia: Elsevier Science; 2005:359–376.

A.10. Would there be any differences in preoperative factor replacement therapy between a patient with hemophilia A or hemophilia B?

The patient with hemophilia A would need transfusion of factor VIII before surgery to correct factor VIII levels to approximately 100% of normal. Further supplementation should be repeated approximately every 1.5 hours. The patient with hemophilia B would need high initial doses of factor IX because of a low recovery from the extensive distribution of factor IX both intravascularly and extravascularly. In addition, the longer half-life of factor IX (18 to 30 hours) requires less frequent dosing.

Table 31.2 Specific Components Measured by Different Coagulation Tests

LABORATORY TESTS	COMPONENTS MEASURED
Bleeding time	Platelet count, vascular integrity
Prothrombin time	I, II, V, VII, and X
Partial prothrombin time	I, II, V, VII, IX, X, XI, and XII
Thrombin time	I, II

Lofqvist T, Nilsson I, Petersson C. Orthopaedic surgery in hemophilia. *Clin Ortho Rel Res.* 1996;332:232–241.

Hines RL, Marschall KE, eds. Stoelting's *Anesthesia and Co-existing Disease.* 5th ed. Philadelphia: Churchill Livingstone; 2008:???.

B. Preoperative Evaluation and Preparation

B.1. What steps would you take to correct this patient's coagulation status before surgery?

Orthopedic surgical procedures requiring more factor replacement than might be expected are those in which a raw bone surface must heal or a small amount of bleeding into or around a prosthetic joint could lead to infection and destruction of the surrounding tissue. In contrast, when the extremity or operative site can be held firm with plaster, or if good surgical apposition of tissues can be achieved with sutures, less factor replacement is required. Factor VIII levels of 30% of normal will usually provide adequate hemostasis; nevertheless, most clinicians will correct abnormal factor VIII levels to normal levels.

For a major orthopedic procedure, the factor VIII level should be corrected to 100% of normal approximately 1 to 2 hours before the procedure. A repeat dose should be given if the surgical procedure lasts more than 1.5 hours or if the measured factor VIII level falls below 40% of normal.

Lofqvist T, Nilsson I, Petersson C. Orthopaedic surgery in hemophilia. *Clin Ortho Rel Res.* 1996;332:232–241.

B.2. What is meant by 1 unit of factor VIII clotting activity and how much does 1 unit of factor VIII clotting activity per kilogram of body weight increase factor VIII concentrations?

One unit of factor VIII clotting activity is defined as the amount present in 1 cc of fresh normal, pooled plasma. A single unit of factor VIII clotting activity per kilogram of body weight will increase plasma factor VIII levels approximately 2%. Therefore, to prescribe the factor VIII activity necessary to correct a 70-kg hemophilia patient with 5% factor VIII activity to 95% of normal, one would calculate as follows:

$$\frac{95\% - 5\%}{2\%} \times 70\text{kg} = 3{,}150 \text{ units of factor VIII}$$

Fauci AS, Braunwald E, Kasper DL, et al., eds. *Harrison's Principles of Internal Medicine.* 17th ed. New York: McGraw-Hill; 2008:726.

Pisciotto, PT. *Blood Transfusion Therapy: A Physician's Handbook.* 4th ed. Bethesda: American Association of Blood Banks, 1993.

B.3. Would you administer factor VIII using a bolus or infusion technique?

Factor VIII concentrates are very stable at room temperature after reconstitution and therefore are appropriate for infusion use. By titrating the infusion, the desired factor VIII level can be maintained, eliminating both the overshoot and the subtherapeutic levels seen with the bolus technique. Although the infusion technique requires close observation, less total factor VIII is infused and therapeutic levels are maintained.

Fauci AS, Braunwald E, Kasper DL, et al. eds. *Harrison's Principles of Internal Medicine*. 17th ed. New York: McGraw-Hill; 2008:726–727.

Schulman S, Gitel S, Martinowitz U. The stability of factor VIII concentrates after reconstitution. *Am J Hematol*. 1994;45:217–223.

Schulman S, Martinowitz U. Continuous infusion instead of bolus injections of factor concentrate? *Haemophilia*. 1996;2:189–191.

B.4. Can a hemophiliac patient fail to mount an appropriate coagulation response following factor VIII infusion?

Approximately 10% to 20% of hemophiliacs will develop an antibody inhibitor against factor VIII and will not achieve the anticipated response following factor VIII infusion.

Hines RL, Marschall KE, eds. Stoelting's *Anesthesia and Co-existing Disease*, 5th ed. Philadelphia: Churchill Livingstone, 2008:421.

B.5. If a patient with hemophilia does not respond to a bolus injection of factor VIII, can an infusion technique be effective?

Some patients who do not respond well to bolus injections may have measurable low titers of inhibitors. A continuous infusion has proved effective in this situation to stop hemorrhage, because appropriate levels of the missing factor can be achieved relatively easily by the infusion method. Those patients with high titers and without measurable factor level during the infusion have also been known to stop bleeding with an infusion technique, likely because complete inhibition of the factor occurs only after 1 to 2 hours. If the factor is continuously infused, there will always be some that is circulating, unneutralized, and hemostatically active.

Fauci AS, Braunwald E, Kasper DL, et al., eds. *Harrison's Principles of Internal Medicine*. 17th ed. New York: McGraw-Hill, 2008:419t, 726–727.

Gordon EM, Mungo R, Goldsmith JG. Lingual hemorrhage in a patient with hemophilia A complicated by a high titer inhibitor. *Am J Pediatr Hematol Oncol*. 1993;15:107–110.

Schulman S, Martinowitz U. Continuous infusion instead of bolus injections of factor concentrate? *Haemophilia*. 1996;2:189–191.

B.6. How much factor VIII activity is present in fresh frozen plasma (FFP)? What are the risks associated with administration of FFP?

FFP is prepared from a single donor and contains all plasma proteins, including factor VIII. Factor VIII activity is between 0.7 and 0.9 units of clotting activity per milliliter of FFP. Following blood donation and plasma separation, approximately 200 mL of FFP is extracted.

The risks associated with the transfusion of FFP are similar to those with any other single donor blood product. These include associated blood proteins and infectious processes such as hepatitis B and C and HIV. The incidence of transfusion-related infections has decreased over the years as screening procedures improved. Currently, the risk of transmitting hepatitis B infection following transfusion of FFP exceeds that of HIV and hepatitis C. The decrease in transfusion-related hepatitis C was secondary to nucleic acid testing, which was initiated in 1999. Hepatitis B currently occurs at a frequency of 1/60,000 to 1/200,000, and hepatitis C occurs at 1/800,000 to 1/1,600,000. HIV infection currently occurs at 1

per 1.5 to 2 million donor exposures. Current techniques for preparation of FFP, including heat, detergent treatments, and monoclonal antibody purifications, can minimize or eliminate the risk of viral pathogen transmission. Some risks associated with transfusion are not related to transmission of infectious organisms. These include transfusion-related acute lung injury (TRALI), which occurs with an incidence of 1/5000 units transfused and is more commonly seen after transfusion of FFP than other blood products. The incidence of TRALI after FFP transfusion is suspected to decrease with the introduction of male-only plasma donors. Multiparous female donors have been excluded from the donor pool because the antibodies in their plasma (anti-human leukocyte antigen and others) attack recipient antigens and are felt to be a cause of TRALI. Other aspects of immune modulation are seen after transfusion and may increase the risk of infection and postoperative complications.

ASA Task Force. Practice guidelines for perioperative blood transfusions and adjuvant therapies: an updated report by the American Society of Anesthesiologists Task Force on perioperative blood transfusions and adjuvant therapies. *Anesthesiology.* 2006;105:198–208.

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia.* 6th ed. Philadelphia: Lippincott Williams & Wilkins, 2009:370–374.

Goodnough LT. Risk of blood transfusion. *Anesthesiol Clin North Am.* 2005;23:241–252.

Spahn DR, Casutt M. Eliminating blood transfusions: new aspects and perspectives. *Anesthesiology.* 2000;93:244–255.

B.7. What are the indications for the administration of FFP?

The National Institute of Health multidisciplinary consensus development panel determined that FFP was the most overused blood product for transfusion. Many clinicians have used FFP as a volume expander; nevertheless, indications for its use should be limited to documented evidence of isolated factor deficiency, reversal of antithrombin III deficiency, selected immunodeficiency's, thrombocytopenia purport, and massive blood transfusion.

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia.* 6th ed. Philadelphia: Lippincott Williams & Wilkins, 2009:380–381.

B.8. How is cryoprecipitate prepared? What are the components in cryoprecipitate? How much factor VIII activity is present in cryoprecipitate? What are the indications for cryoprecipitate?

Cryoprecipitate is the fraction of plasma that precipitates when FFP is thawed. In addition to factor VIII, this solution also contains significant levels of factor VIII: vWF, factor XIII, and fibrinogen. This product contains high concentrations of factor VIII in a small volume, usually between 5 and 13 units of factor VIII clotting activity per milliliter.

Cryoprecipitate is indicated for patients with hemophilia, vWD, hypofibrinogenemia, as well as uremic platelet dysfunction. Small amounts of red cell fragments may be present in cryoprecipitate; therefore, it may sensitize Rh-negative individuals to the Rh antigens if the donor is Rh positive.

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia.* 6th ed. Philadelphia: Lippincott Williams & Wilkins, 2009:386.

Hines RL, Marschall KE, eds. Stoelting's *Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone, 2008:420–421.

Tetit CR, Klein HG. *Hemophilia, Hemophiliacs and the Health Care Delivery System*. Department of HEW Publication No. (NIH) 76-871. Bethesda, MD: National Institutes of Health; 1976:31.

B.9. Describe the advantages and disadvantages of the products that are available for transfusion of factor VIII activity.

The advantages and disadvantages of factor VIII products are shown in Table 31.3.

Fauci AS, Braunwald E, Kasper DL, et al., eds. *Harrison's Principles of Internal Medicine*. 17th ed. New York: McGraw-Hill; 2008:726–727.

Schulman S, Varon D, Keller N, et al. Monoclonal purified FVIII for continuous infusion: stability, microbiological safety, and clinical experience. *Thromb Haemostas*. 1994;72:403–407.

White GC, McMillan CW, Kindon HS. The use of recombinant antihemophilic factor in the treatment of two patients with classic hemophilia. *N Engl J Med*. 1989;320:154.

B.10. What is the role of desmopressin D-arginine vasopressin (DDAVP) for hemostatic management in this patient?

This synthetic analog of the antidiuretic hormone is used to prepare patients with mild and moderate hemophilia for minor surgery. Intravenous DDAVP will rapidly release preformed factor VIII complex, which leads to a twofold to threefold increase in circulating factor VIII within 30 to 60 minutes of administration. In addition, factor VIII and vWF are released from the endothelial cells. In a patient with mild or moderate hemophilia A or vWD, this influx of factor VIII may provide adequate hemostasis for minor elective surgical procedures. The half time of this released factor is approximately 12 hours, and repeated administration of DDAVP will deplete the storage capacity in the endothelial cells.

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins, 2009:404–405.

Hines RL, Marschall KE, eds. Stoelting's *Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone, 2008:427–428.

Table 31.3 The Advantages and Disadvantages of Factor VIII Products

COMPONENT	ADVANTAGE	DISADVANTAGE
Cryoprecipitate	Readily available, long shelf life, relatively low risk for hepatitis and AIDS	Allergic reaction, hyperfibrinogenemia if large volumes are used
Factor VIII concentrates	Easily stored and reconstituted, long life, known potency	Multiple plasma product with high risk of infectious disease
Monoclonal purified factor VIII	Stability, biologic safety	Cost (?)
Recombinant Factor VIII	Easily stored, reconstituted, long shelf life, +/− less risk for developing inhibitors	Allergic hypersensitivity Cost

B.11. What is the role of ε-aminocaproic acid (EACA) in the perioperative period for the patient with hemophilia?

EACA is an antifibrinolytic that has been used successfully in patients with hemophilia to prevent bleeding following minor surgical procedures. Its use in major surgical procedures has not been well documented. If DDAVP is to be used preoperatively, the release of plasminogen activator by DDAVP mandates the use of EACA as well.

Barash PG, Cullen BF, Stoelting RK, et al. eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins, 2009:405.

B.12. Is there a role for recombinant activated factor VII (rFVIIa) in the treatment of hemophilia?

Hemophilia A represents the majority of patients afflicted with hemophilia. Approximately 30% of patients with hemophilia A have inhibitory antibodies ("inhibitors") to FVIII. Fewer patients afflicted with hemophilia B develop inhibitory antibodies (1% to 3%). Risk factors for the development of "inhibitors" include race, severity of the disease (less than 1% FVIII levels), having a hemophiliac brother with "inhibitors," and certain mutations involving the FVIII gene. In patient's with "inhibitors," alternative treatment is occasionally necessary to address surgical and nonsurgical hemorrhagic crises. The U.S. Food and Drug Admininstration has approved the use of rFVIIa (NovoSeven, Novo Nordisk, Bagsvaerd, Denmark) in patients afflicted with hemophilia and inhibitory antibodies who experience a bleeding episode. Some studies have highlighted the effectiveness of rFVIIa for establishing hemostasis in this patient population.

Hedner U. Treatment of patients with factor VIII and factor IX inhibitors with special focus on the use of recombinant factor VIIa. *Thromb Haemost*. 1999;82:531–539.

High KA. Factor IX: molecular structure, epitopes, and mutations associated with inhibitor formation. In: Aledort LM, Hoyer LW, Lusher JM, et al., eds. *Inhibitors to Coagulation Factors*. New York: Plenum Press; 1995:79–86.

Hoyer LW. The incidence of factor VIII inhibitors in patients with severe haemophilia A. In: Aledort LM, Hoyer LW, Lusher JM, et al., eds. *Inhibitors to Coagulation Factors*. New York: Plenum Press; 1995:35–45.

Ingerslev J. Efficacy and safety of recombinant factor VIIa in the prophylaxis of bleeding in various surgical procedures in hemophilic patients with factor VIII and factor IX inhibitors. *Semin Thromb Hemost*. 2000;26:425–432.

Negrier C, Hay CR. The treatment of bleeding in hemophilic patients with inhibitors with recombinant factor VIIa. *Semin Thromb Hemost*. 2000;26:407–412.

B.13. What is the mechanism and dosing of rFVIIa?

Factor VIIa binds to TF exposed at the site of injury and generates enough thrombin to activate factors V, VIII, and XI, as well as platelets. In high doses, rFVIIa binds to thrombin-activated platlets and activates factor X independent of factor VIII or IX. This mechanism of activating factor X and generating thrombin bypasses the need for FVIII and FIX. This alternative pathway for providing hemostasis makes rFVIIa a potent treatment for patients afflicted by hemophilia with "inhibitors." The typical doing schedule for hemostatic prophylaxis in patients undergoing elective surgery is 90 to 120 μg/kg, with repeated doses every 2 to 3 hours. This dosing regimen has been

shown to be effective 90% of the time in treating mild to moderate bleeding episodes in patients with hemophilia patients with "inhibitors." Recent studies support the use of larger bolus doses of rFVIIa (greater than 200 μg/kg) in patients experiencing more significant bleeding. The increased dosing of rFVIIa is thought to enhance thrombin generation on activated platelets and thus promote the formation of a more stable fibrin clot.

Abshire T, Kenet G. Safety update on the use of recombinant VIIa and the treatment of congenital and acquired deficiency of factor VIII or IX with inhibitors. *Haemophilia*. 2008;14:898–902.

Abshire T, Kenet G. Recombinant factor VIIa review of efficacy, dosing regimens and safety in patients with congenital and acquired factor VIII or IX inhibitors. *J Thromb Haemost*. 2004;2:899–909.

Hedner U. Potential role of rFVIIa in prophylaxis in severe haemophilia patients with inhibitors. *J Thromb Haemost*. 2006;4:2498–2500.

Hedner U. Mechanism of action, development and clinical experience of recombinant FVIIa. *J Biotechnol*. 2006;124:747–757.

Shapiro AD, Gilchrist GS, Hoots WK, et al. Prospective, randomized trial of two doses of rFVIIa (NovoSeven) in haemophilia patients with inhibitors undergoing surgery. *Thromb Haemost*. 1998;80:773–778.

C. Intraoperative Management

C.1. Is it safe to administer an intramuscular injection to this patient before surgery?

Intramuscular injections can be safely administered to any patient with a factor VIII activity greater than 30%. Therefore, if appropriate factor VIII correction has occurred before surgery, an intramuscular injection would be considered safe. It is unlikely, though, that an intramuscular injection would be necessary for this patient. If a sedative hypnotic or anticholinergic drug would be necessary before the induction of anesthesia, it would be prudent to use an intravenous route.

Hines RL, Marschall KE, eds. Stoelting's *Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone; 2008:420–421.

C.2. Would an axillary block be appropriate for this patient?

Regional anesthesia has long been considered contraindicated in patients with hemophilia because the concern of hematoma formation at the regional site. With proper management of the coagulation status, regional techniques have been successfully performed in patients with hemophilia. As with any patient, the benefit of regional technique must be weighed against the potential risk associated with this technique. Certainly, in a patient with a full stomach, a regional technique might be more appropriate because of the relative risk of aspiration. For a completely elective procedure in the patient with hemophilia, a more prudent course might be general anesthesia.

Sampson JF, Hamstra R, Aldrete JA. Management of hemophiliac patients undergoing surgical procedures. *Anesth Analg*. 1979;58:133–135.

C.3. If general anesthesia is used as a technique, would it be safe to intubate the patient's trachea?

Airway management of the patient with hemophilia presents a unique challenge for the anesthesiologist because of the risk of hemorrhage in the tongue or neck, which could completely compromise the upper airway of the patient. Therefore, manipulation of the airway during intubation should not be performed until appropriate replacement factors have been administered. Care should be used in placing the mask on the patient to avoid trauma to the lips, tongue, or face; elective laryngoscopy should be attempted only following preoperative factor correction and achievement of complete muscle relaxation. A smaller than predicted well-lubricated endotracheal tube should be used for intubation, and nasal intubation, with its propensity for epistaxis, should be avoided.

Bogdan CJ, Strauss M, Ratnoff OD. Airway obstruction in hemophilia (factor VIII deficiency): a 28-year institutional review. Laryngoscope 1994;104:789–794.

C.4. Would you use any special precautions for this patient who is positive for HIV?

Standard precautions should be used for all patients regardless of their HIV status. Strict attention to aseptic technique throughout the surgical procedure should be emphasized (postoperative infections are more common in HIV-positive patients undergoing orthopedic procedures such as these).

Hines RL, Marschall KE, eds. Stoelting's *Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone, 2008:419–421.

Thomason HC 3rd, Wilson FC, Lachiewiczpf PF, et al. Knee arthroplasty in hemophiliac arthropathy. *Clin Ortho*. 1999;360:169–173.

C.5. What special considerations should be taken in choosing anesthetic drugs for this patient?

Coexisting liver disease is a common complication in the patient with hemophilia as a result of hepatitis acquired from previous blood or factor transfusions. As a result, drugs that are metabolized by the liver should be used with caution in these patients. A balanced intravenous technique might be preferable to an inhaled anesthetic because of the reduced hepatic blood flow observed in an inhaled technique.

Hines RL, Marschall KE, eds. Stoelting's *Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone, 2008:419–421.

C.6. During the operative procedure, the surgeon indicated that significant blood loss had occurred. Would you transfuse this patient with packed red blood cells or whole blood?

In general, blood banks will fractionate donated blood into component parts, allowing individual transfusion of red cells, platelets, FFP, or cryoprecipitate. Following blood loss, oxygen-carrying capacity and volume expansion are required and usually packed red blood cells and a salt solution are sufficient. In a patient with hemophilia, transfusion of packed red blood cells will further dilute already depressed circulating

factor VIII levels; therefore, transfusion of whole blood in such a patient, if it can be obtained, would be appropriate. With this technique, both oxygen carrying capacity and all components of coagulation will be replenished.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone, 2010:1758.

C.7. During the transfusion of the first unit of whole blood, the patient's temperature rose from 36.8° C to 37.9° C (98.24° F to 100.22° F). What immediate steps should be taken by the anesthesiologist at this time?

Ruling out an acute hemolytic transfusion reaction should always be considered when a patient becomes febrile during a blood transfusion. The anesthesiologist should immediately discontinue the transfusion, and blood should be drawn from the patient and sent to the blood bank with the questionable unit of blood to allow further cross-matching. An additional tube of blood should be collected and allowed to sit undistributed for 5 to 10 minutes, allowing separation of red cells from plasma. The presence of free plasma hemoglobin in the serum is diagnostic of a hemolytic reaction. In the presence of an acute hemolytic blood transfusion reaction, profound hypotension requiring the use of vasopressors is likely. Fluid and diuretic therapy may be required to maintain renal function. A febrile reaction that is not due to an acute hemolytic transfusion reaction can occur with blood transfusion; these are usually self-limited. Once a transfusion reaction is ruled out, further investigation of the increase in temperature is warranted.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone, 2010:1752–1754.

C.8. Does giving blood intraoperatively increase the potential for the development of factor VIII inhibitors?

Although 10% to 30% of all patients with hemophilia will develop a circulating inhibitor of factor VIII, no evidence has been demonstrated that development of such an inhibitor is related to the number of transfusions that the patient receives. As a result, the administration of blood products in this setting should not be withheld for fear of inducing an inhibitor response.

Rodriguez-Merchan EC, Christine A. Lee. Inhibitors in Patients with Haemophilia, 2002:17–19.

C.9. Can factor VIII be safely administered to patients who have developed circulating inhibitors?

Occasionally, patients with the most severe variance of hemophilia (factor levels less than 1%) develop immunoglobulin G antibodies to the deficient factor. The inhibitors may be of low titer and transient or of extremely higher titer and very persistent. The "Bethesda unit" of inhibition is defined as the amount of inhibitory activity in 1 mL of plasma that decreases the factor VIII level in 1 mL of normal plasma from 1 to 0.5 units. It is almost impossible to overpower a high-titer inhibitor, but, when life-threatening hemorrhage occurs, massive doses of factor VIII concentrates or plasmapheresis with replacement of factor VIII can be given and

may be of temporary benefit. Replacement with large amounts of factor VIII concentrate may provide temporary hemostasis but will stimulate an increase in the antibody titer. Porcine factor VIII may provide hemostasis because of its distinct antigenicity, even in the presence of circulating inhibitor. Immunosuppressive therapy is of no value.

Alternative approaches to therapy of the hemophilic patient with inhibitors involve the use of other agents, such as activated prothrombin complex concentrated, which contain activated vitamin K–dependent enzymes as well as recombined factor VIIa. These activated coagulants enter the coagulation cascade distal to the level of factor VIII and therefore bypass the effects of the inhibitor. Factor eight inhibitor bypass activity is one such prothrombin complex concentrate that is used in the United States to treat hemophilia with inhibitors. Thrombosis is a possible complication when using activated prothrombin complex concentrated.

Porcine factor VIII is effective in patients with hemophilia with inhibitors. The porcine factor VIII provides adequate factor VIII activity in patients with less than 50 Bethesda units of inhibitor. The usual starting dose is 100 to 150 porcine units per kg.

Behrman RE, Kliegman RM, Jenson HB, eds. *Nelson Textbook of Pediatrics*. 16th ed. Philadelphia: WB Saunders; 2000:1508–1511.

DiMichele D. Hemophilia. *Pediatr Clin North Am.* 1996;43:709.

Perkins JT, Vender JS. Transfusion therapy. In: Collins VJ, ed. *Physiologic and Pharmacologic Bases of Anesthesia*. Baltimore: Williams & Wilkins; 1996:219–221.

C.10. The surgeon has requested the use of a tourniquet to minimize surgical bleeding. What are the physiologic and hemodynamic responses to tourniquet use?

Although the tourniquet will provide optimal surgical conditions, the physiologic and hemodynamic consequences are significant. Anaerobic metabolism distal to the tourniquet begins approximately 8 minutes after inflation; a decrease in nicotinamide adenine dinucleotide and creatine phosphate stores in muscle will occur over the next 30 to 60 minutes. As a result, cellular acidosis will cause the release of myoglobin, intracellular enzymes, and potassium. In addition, the limb loses internal heat and may approach room temperature.

Hemodynamic changes are seen when the tourniquet is inflated and deflated. Exsanguination of the limb and tourniquet inflation expands central venous blood volume, which may have significant hemodynamic consequences in a patient with limited cardiac reserve. Tourniquet deflation and reperfusion of the limb can be associated with profound decreases in central venous and arterial blood pressure, as a result in a decrease in vascular resistance with the washout of metabolites produced during the ischemic period. Prolonged inflation (greater than 45 to 60 minutes) can result in systemic hypertension for reasons that are likely due to the presence of a critical level of ischemia in the muscle or nerve.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone, 2010:2252.

C.11. Is it appropriate to suction the endotracheal tube and oropharynx of this patient before extubation?

Removal of secretions that might be aspirated is essential before the extubation of any patient; nevertheless, suctioning of the oropharynx of hemophiliac patient can trap

mucosa in the suction catheter and result in the formation of an oral hematoma. In a patient with hemophilia, gentle oral suctioning under direct vision is appropriate to remove all secretions.

Hyderally H, Stark DCC. Hemophilia: anesthetic implications. *Mt. Sinai J Med.* 1977;44:397–399.

D. Postoperative Management

D.1. What special consideration should be given to postoperative pain management for this patient?

It is important to avoid any postoperative pain supplements that might produce a bleeding diathesis in the patient with hemophilia. Analgesics containing aspirin or nonsteriodal anti-inflammatory drugs should obviously be avoided. Antihistamines and antitussives can inhibit platelet aggregation and prolong bleeding time. Opioid analgesics or acetaminophen-based products should be appropriately titrated for postoperative pain management. If regional blockade with a catheter technique was used for anesthesia, postoperative analgesics should be administered through this route.

Hilgartner MW. *Factor Replacement in Hemophilia in the Child and Adult*. New York: Masson Publishers; 1983:78.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone, 2010:2762–2764.

D.2. What steps should be taken to enhance the coagulation status of this patient in the postoperative period while at home?

It is important that factor VIII levels are supplemented for at least 2 to 4 weeks following surgery. It has been shown that allowing factor VIII levels to fall to the levels normally associated with these patients can result in postoperative hemorrhage. Postoperatively, many clinicians recommend maintaining levels at 80% of normal for the first 4 postoperative days, whereas others feel that levels of at least 40% of normal are adequate. The consensus is that factor VIII levels on postoperative days 5 to 8 should be maintained at 30% to 40% of normal, whereas levels of 10% to 20% of normal should be maintained for the following 2 to 4 weeks.

Hilgartner MW. *Factor Replacement in Hemophilia in the Child and Adult*. New York: Masson Publishers; 1983:76.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone, 2008:419–421.

Inwood MJ, Meltzer DB. The female carrier of hemophilia: a problem for the anesthetist. *Can Anaesth Soc J*. 1978;25:266–269.

Lofqvist T, Nilsson I, Petersson C. Orthopaedic surgery in hemophilia. *Clin Ortho Rel Res.* 1996;332:232–241.

D.3. Can this patient be treated with factor VIII supplements using home infusion?

Administration of factor VIII concentrate by continuous infusion is routinely used at medical centers for postoperative patients with hemophilia being treated on an inpatient basis. In the transition of many surgical procedures to the outpatient arena, home infusion of factor VIII can provide the same level of hemostatic protection. Home infusion of purified factor VIII concentrate has been shown to be safe, efficacious, and convenient for postoperative patients and should be used for this patient.

Lee CA, Berntop EE, Hoots WK. *Textbook of Hemophilia*. New York: Wiley 2010:48–51.

Varon D, Schulman S, Bashari D, et al. Home therapy with continuous infusion of factor VIII after minor surgery or serious hemorrhage. *Hemophilia*. 1996;2: 207–210.

CHAPTER 32

Sickle Cell Disease

CHRIS R. EDMONDS AND VINOD MALHOTRA

A 30-YEAR-OLD AFRICAN-AMERICAN WOMAN with avascular necrosis of her right hip was admitted for a total hip arthroplasty. Her hematocrit was 22%, blood pressure was 130/90 mm Hg, and pulse was 107 beats per minute. She has a past medical history of recurrent joint pain, bone pain, jaundice, and abdominal pain requiring multiple hospitalizations for analgesia. Her past surgical history was remarkable for a cholecystectomy, and her postoperative course was remarkable for a prolonged hospitalization for respiratory complications.

A. Medical Disease and Differential Diagnosis

1. What was the most likely underlying medical problem in this patient? How would you confirm the diagnosis of sickle cell anemia (SCA)?
2. What is sickle cell disease (SCD)?
3. What is sickle cell trait (SCT)?
4. What are some of the other hemoglobinopathies and what are their clinical features?
5. What are the clinical features of SCD?
6. Describe the different types of sickle cell crises.
7. Discuss the pathophysiologic effects of SCD.
8. What is acute chest syndrome?

B. Preoperative Evaluation and Preparation

1. What preoperative evaluation would you perform on this patient before anesthesia?
2. How would you prepare this patient for general anesthesia and regional anesthesia?
3. Discuss the indications for preoperative exchange transfusion in this patient.
4. What are the indications for blood transfusion in SCD?

C. Intraoperative Management

1. Discuss the anesthetic management for this patient. Discuss both regional and general anesthesia considerations.
2. Discuss how the comorbidities associated with SCD can affect your anesthetic management.
3. What precautions should one take to prevent sickling in this patient?

D. Postoperative Management

1. Discuss the postoperative management of this patient.
2. What complications might occur in this patient in the immediate postoperative period?
3. What is the treatment of sickle cell crisis?
4. What is the role of hyperbaric oxygen therapy in treatment of sickle cell crisis?

A. Medical Disease and Differential Diagnosis

A.1. What was the most likely underlying medical problem in this patient? How would you confirm the diagnosis of sickle cell anemia (SCA)?

For a young African-American patient presenting with a history of joint pain, bone pain, abdominal pain, and anemia, the most likely diagnosis is SCD. Other diagnoses to consider include other hemoglobinopathies, dermatomyositis, glucose-6-phosphate dehydrogenase (G6PD) deficiency, and porphyria. Nevertheless, given the constellation of symptoms and the laboratory findings, SCD is the most likely diagnosis. A hemoglobin (Hgb) electrophoresis will confirm the diagnosis and provide the percentage of abnormal hemoglobin S (HgbS).

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:634–636.

Firth PG. Anaesthesia for peculiar cells: a century of sickle cell disease. *Br J Anaesth*. 2005;95:287–299.

Firth PG. Anesthesia and hemoglobinopathies. *Anesthesiol Clin*. 2009;27:321–336. doi:10.1016/j.anclin.2009.05.001.

A.2. What is sickle cell disease (SCD)?

SCD is a hereditary hemoglobinopathy resulting from inheritance of a *β-globin* gene mutation located on chromosome 11. This mutation leads to a single-point mutation where adenine is replaced with thymine. The mutant β-allele codes for production and assembly of a variant Hgb (β-S). The molecular basis of SCD has been demonstrated to be the substitution of valine for glutamic acid in the sixth position from the *N*-terminus of the β-chains of Hgb. This substitution replaces a hydrophilic negative-charged amino acid (glutamic acid) with a hydrophobic nonpolar amino acid (valine). This greatly destabilizes the structure of Hgb and exposes highly reactive hydroxyl groups on the protein surface. The mutation in β-S Hgb accelerates the denaturation of the Hgb molecule and significantly decreases its solubility. Decreased oxygen tension causes conformational changes in the Hgb molecule, allowing hydrophobic bonds to form between the BS-6 valine of one chain and the BS-85 phenylalanine and the BS-88 leucine of a second chain. This bond forms insoluble tetramers that bond with other tetramers to form long helical strands that subsequently polymerize, causing deformation of the red blood

cell membrane into a sickle shape. The result is a red blood cell that is less able to transverse the capillaries of the microcirculation, disposing the end organ to hypoxia and ischemic damage when sickle cells are present in sufficient quantity. In the United States, the estimated prevalence of Hgb SS disease is 1:625 (0.2%) in people of African descent. Patients with SCA have early mortality, with the median age of death in the late 40s to early 50s.

Bunn HF. Pathogenesis and treatment of sickle cell disease. *N Engl J Med.* 1997;337:762–769.

Danzer BI, Birnbach DJ, Thys DM. Anesthesia for the parturient with sickle cell disease. *J Clin Anesth.* 1996;8:598–602.

Firth PG. Anaesthesia for peculiar cells: a century of sickle cell disease. *BJA.* 2005;95:287–299.

Firth PG. Anesthesia and hemoglobinopathies. *Anesthesiol Clin.* 2009;27:321–336. doi:10.1016/j.anclin.2009.05.001.

Firth PG, Head A. Sickle cell disease and anesthesia. *Anesthesiology.* 2004;101:766–785.

Gregory GD, ed. *Pediatric Anesthesia.* 4th ed. New York: Churchill Livingstone; 2002:140–142.

Lane PA. Sickle cell disease. *Pediatr Clin North Am.* 1996;43:639–664.

Roth EF, Elbaum D, Bookchin RM, et al. The conformational requirements for the mechanical precipitation of hemoglobin S and other mutants. *Blood.* 1976;48:265–271.

Steinberg MH. Management of sickle cell disease. *N Engl J Med.* 1999;340:1021–1030.

A.3. What is sickle cell trait (SCT)?

SCT is the heterozygous or carrier state of SCD. Large-scale screening for SCD in American military recruits revealed an incidence of SCT (HbAS) of 8% to 10% in African-Americans and 0.05% to 0.08 % in others. HbAS cells begin to sickle only when oxygen saturation of Hgb is less than 20%. No difference has been found between normal persons (HbAA) and those with HbAS regarding survival rates or incidence of severe disease, with one exception: patients with HbAS have a 50% increased risk for pulmonary infarctions. Studies have suggested that SCT provides a survival advantage over hematologic normal individuals when infected by the malarial parasite *Plasmodium falciparum*.

Allison AC. Protection afforded by sickle cell trait against subtertian malarial infection. *Br Med J.* 1954;1:290–294.

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia.* 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:634–636.

Firth PG. Anaesthesia for peculiar cells-a century of sickle cell disease. *BJA.* 2005;95:287–299.

Firth PG. Anesthesia and hemoglobinopathies. *Anesthesiol Clin.* 2009;27:321–336. doi:10.1016/j.anclin.2009.05.001.

Firth PG, Head A. Sickle cell disease and anesthesia. *Anesthesiology.* 2004;101:766–785.

Park KW. Sickle cell disease and other hemoglobinopathies. *Int Anesthesiol Clin.* 2004;42:77–93.

A.4. What are some of the other hemoglobinopathies and what are their clinical features?

The most common hemoglobinopathies include the thalassemias, Hgb C disease, and SCA. Thalassemia arises from alterations in one or more of the four genes that

code for the α-chain. The mildest form of thalassemia (loss of one α-gene) presents as a mild form of anemia, whereas the most severe form (loss of all four genes) is incompatible with life. Hgb C results from a mutation in the *β-globin* gene. Hgb C disease is a relatively benign disease producing a mild hemolytic anemia and splenomegaly. However, when it is paired with a β-S mutation, the disease is more severe. Other rare hemoglobinopathies will not be discussed further.

Each Hgb gene mutation of the heterozygous form causes little or no clinical consequence, but when both genes of a heterozygote are abnormal, a disease state is evident. Heterozygous combinations such as HbS and HbC (HbSC disease), and β-thalassemia mutation (HbS-β-thalassemia) usually cause a milder clinical course than that of SCD.

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:634–636.

Bunn HF. Pathogenesis and treatment of sickle cell disease. *N Engl J Med*. 1997;337:762–769.

Firth PG. Anesthesia and hemoglobinopathies. *Anesthesiol Clin*. 2009;27:321–336. doi:10.1016/j.anclin.2009.05.001.

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McGoldrick KE, ed. *Ambulatory Anesthesiology: A Problem-Oriented Approach*. Baltimore: Williams & Wilkins; 1995:68–69.

Park KW. Sickle cell disease and other hemoglobinopathies. *Int Anesthesiol Clin*. 2004;42:77–93.

Steinberg MH. Management of sickle cell disease. *N Engl J Med*. 1999;340:1021–1030.

A.5. What are the clinical features of SCD?

The clinical features of SCD are manifested through indolent end-organ damage with intermittent acute episodes of severe pain and pulmonary complications. Although SCD is a disease of Hgb, it ultimately affects all organ systems. It is usually the acute problems that bring these individuals to the attention of a physician. The clinical manifestations by organ systems are presented in Table 32.1.

The progression and severity of SCD is variable. Many of the patients have an indolent course, whereas a smaller subset suffer from an early end-organ failure and an early death. Pulmonary, neurologic, and renal disease are the leading causes of morbidity and mortality.

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:634–636.

Danzer BI, Birnbach DJ, Thys DM. Anesthesia for the parturient with sickle cell disease. *J Clin Anesth*. 1996;8:598–602.

Firth PG, Head A. Sickle cell disease and anesthesia. *Anesthesiology*. 2004;101:766–785.

Firth PG. Anesthesia and hemoglobinopathies. *Anesthesiology Clin*. 2009;27:321–336. doi:10.1016/j.anclin.2009.05.001.

Firth PG. Anaesthesia for peculiar cells-a century of sickle cell disease. *BJA*. 2005; 95: 287–299.

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Hines RL, Marschall KE, eds. Stoelting's *Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone; 2008:??

McMillan JA, De Angelis CD, Feigin RD, et al., eds. *Oski's Pediatrics: Principles and Practice*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2006.

Table 32. 1 Clinical Manifestations of Sickle Cell Disease

SYSTEM	SYMPTOMS
Central nervous system/neurologic	• Stroke (cerebrovascular accident) in children as well as adults (50%–70% recurrence within 3 years) • Proliferative retinopathy/blindness • Painful crisis • Chronic pain • Peripheral neuropathy • Poor school performance
Cardiovascular	• Conduction abnormalities secondary to iron overload • Hypertension • Cor pulmonale • Left and right ventricular dysfunction • Chronic ulcers
Pulmonary	• Infarction, pulmonary fibrosis • Infection • Restrictive/obstructive lung disease • Acute chest syndrome • Pulmonary hypertension (30%–40%) • Airway hyperactivity
Genitourinary	• Hyposthenuria, hematuria, proteinuria • Chronic renal insufficiency (5%–20 %) • Renal failure • Priapism (10%–40% of men)
Gastrointestinal	• Cholelithiasis (70%) • Acute hepatic syndrome • Elevated liver function tests, hyperbilirubinemia • Hepatopathy • Cirrhosis (16%–29%) • Dyspepsia secondary to mucosal ischemia • Sickle girdle syndrome (mesenteric ischemia)
Musculoskeletal	• Osteomyelitis (*Staphylococcus/Salmonella*) • Dactylitis • Avascular necrosis • Infarction
Heme/immunologic	• Chronic anemia • Autosplenism • Susceptibility to infections with encapsulated organisms • Erythrocyte alloimmunization from blood transfusions • Sequestration crisis • Hemolytic crisis • Aplastic crisis • Immune dysfunction • Hypercoagulability • Chronic inflammation

Table 32.2 Types of Sickle Cell Crises

TYPE	PATHOPHYSIOLOGY	TREATMENT
Vaso-occlusive	Pain secondary to obstruction of flow in the microvascular beds leading to localized ischemia	• Hydration • Analgesia • Incentive spirometry
Splenic sequestration	Acute painful enlargement of the spleen Acute hypovolemia	• Restore circulatory volume, possible splenectomy
Aplastic	Sudden cessation of bone marrow activity Acute worsening of anemia usually associated with viral infection (parvovirus B19) Recovery in 7–10 days	• Supportive therapy • Blood transfusion
Hemolytic crisis	Acute accentuated decrease in hemoglobin level Secondary to red cell destruction Usually associated with coexisting G6PD deficiency	• Supportive therapy • Blood transfusion

G6PD, glucose-6-phosphate dehydrogenase.

A.6. Describe the different types of sickle cell crises.

Sickle cell crisis refers to the acute clinical picture generally caused by sickling of red blood cells in the *microcirculation*. Four main clinical types of crises have been described as follows in Table 32.2.

The most common crises in SCD is vaso-occlusive crisis, which is characterized with intermittent, recurrent acute episodes of severe pain. It is generally felt that the central cause of pain is ongoing acute ischemia, vaso-occlusion, and infarction. The precise pathophysiology and nociceptive pathways have not been elucidated. Patients in vaso-occlusive crisis present with fever, anemia, spine pain, limb pain, and abdominal pain. They are tachypneic and may have an enlarged liver and spleen in addition to abdominal tenderness. Serjent et al. reported that in 118 patients having 183 painful crises, the location was noted to be in the lumbar spine (49%), abdomen (32%), femoral shaft (30%), and the knee (21%). There is usually no identifying triggering agent for most vaso-occlusive crises. The average rate of painful crises per patient year is 0.8%. There is a subset of patients (5.2%) who average 8 to 10 crises a year, which accounts for 33% of all hospitalizations. Mortality positively correlates with increased pain rate in adults.

Firth PG, Head A. Sickle cell disease and anesthesia. *Anesthesiology.* 2004;101:766–785.

Firth PG. Anesthesia and hemoglobinopathies. *Anesthesiol Clin.* 2009;27:321–336. doi:10.1016/j.anclin.2009.05.001.

Lane PA. Sickle cell disease. *Pediatr Clin North Am.* 1996;43:639–664.

Serjent GR, Ceulaer CD, Lethbridge R, et al. The painful crises of homozygous sickle cell disease: clinical features. *Br J Haematol.* 1994;87:586–591.

Vijay V, Cavenagh JD, Yate P. The anaesthetist's role in acute sickle cell crisis. *Br J Anaesth.* 1998;80:820–828.

A.7. Discuss the pathophysiologic effects of SCD.

The pathophysiologic effects of SCD is not limited to the structure or deformation of the erythrocyte. The interaction and balance between the Hgb molecule,

cytoplasm, and cell wall and the vascular endothelium is drastically altered to create chronic systemic biochemical alterations that produce the clinical features of SCD. As in vaso-occlusive crisis, there is a triggering insult, such as infection, surgical stress, or ischemia-reperfusion injury, that catalyzes a complex interaction among sickled cells, endothelial regulation of flow, inflammatory cytokines, platelet aggregation factors, and vasoconstriction, leading eventually to ischemia, infarction, and cell death. This cascade leads to a vicious cycle that eventually causes end-organ damage and dysfunction. End-organ damage that occurs in sickle cell states is attributable to three pathways. In the erythrocyte cytoplasm, the loss of Hgb structural stability leads to increased oxidation of heme with subsequent denaturation, deterioration, and polymerization. Iron oxidation produces superoxides (O_2^-) and hydrogen peroxides ($H_2O_2^-$), which increases the formation of highly reactive hydroxyl radicals($-OH$). In the cell membrane, free iron and iron-containing compounds accumulate, leading to clustering of membrane surface membranes, abnormal cation permeability, and cellular dehydration. This complex series of events within the erythrocyte increases adherence to the vascular endothelium, exposing it to shear and oxidative stress. The interaction between the abnormal erythrocytes and the vascular endothelium produces chronic inflammation, upregulation of endothelial cell adhesion molecules and altered expression of endothelial nitric oxide synthetase. Systemically, there is an increase in leukocyte counts, activation of the coagulation pathways, increase in inflammatory compounds, and increase in circulating endothelial cells in the plasma. The complex pathologic interaction between sickling of cells in blood vessels and the vascular endothelium leads to infarcts, tissue destruction, and consequent end-organ failure. The pathogenesis is shown in Figure 32.1.

Firth PG. Anesthesia and hemoglobinopathies. *Anesthesiology Clin.* 2009;27:321–336. doi:10.1016/j.anclin.2009.05.001.

Firth PG. Anaesthesia for peculiar cells: a century of sickle cell disease. *BJA*. 2005;95:287–299.

Head CA, Brugnara C. Low concentrations of nitric oxide increase affinity of sickle erythrocytes in vitro and in vivo. *J Clin Invest*. 1997;1193–1198.

Bunn HF. Pathogenesis and treatment of sickle cell disease. *N Engl J Med.* 1997;337:762–769.

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Vijay V, Cavenagh JD, Yate P. The anaesthetist's role in acute sickle cell crisis. *Br J Anaesth.* 1998;80:820–828.

A.8. What is acute chest syndrome?

Acute chest syndrome is a term used to describe an acute pulmonary complication of SCD. It is defined by the finding of a new pulmonary infiltrate involving at least one complete lung segment on chest radiograph that is not due to atelectasis. It presents with a constellation of pulmonary symptoms and signs in a patient with SCD. These include fever (temperature 38.5° C [101.3° F]), wheezing, coughing, tachypnea, chest pain, and hypoxemia (less than 92% on room air). Pleural effusions (55%) are commonly seen on chest radiographs. Acute chest syndrome frequently follows vaso-occlusive crises; therefore, vaso-occlusive pulmonary infarction may be a precipitating factor. Other causes include infection (viral, chlamydia, mycoplasma, and bacterial) and pulmonary fat embolism resulting from bone marrow necrosis. Acute chest syndrome is a common postoperative complication in patients with SCD who have a history of pulmonary disease following general anesthesia. It is one of the most common causes of death in adults with SCD. Acute chest syndrome

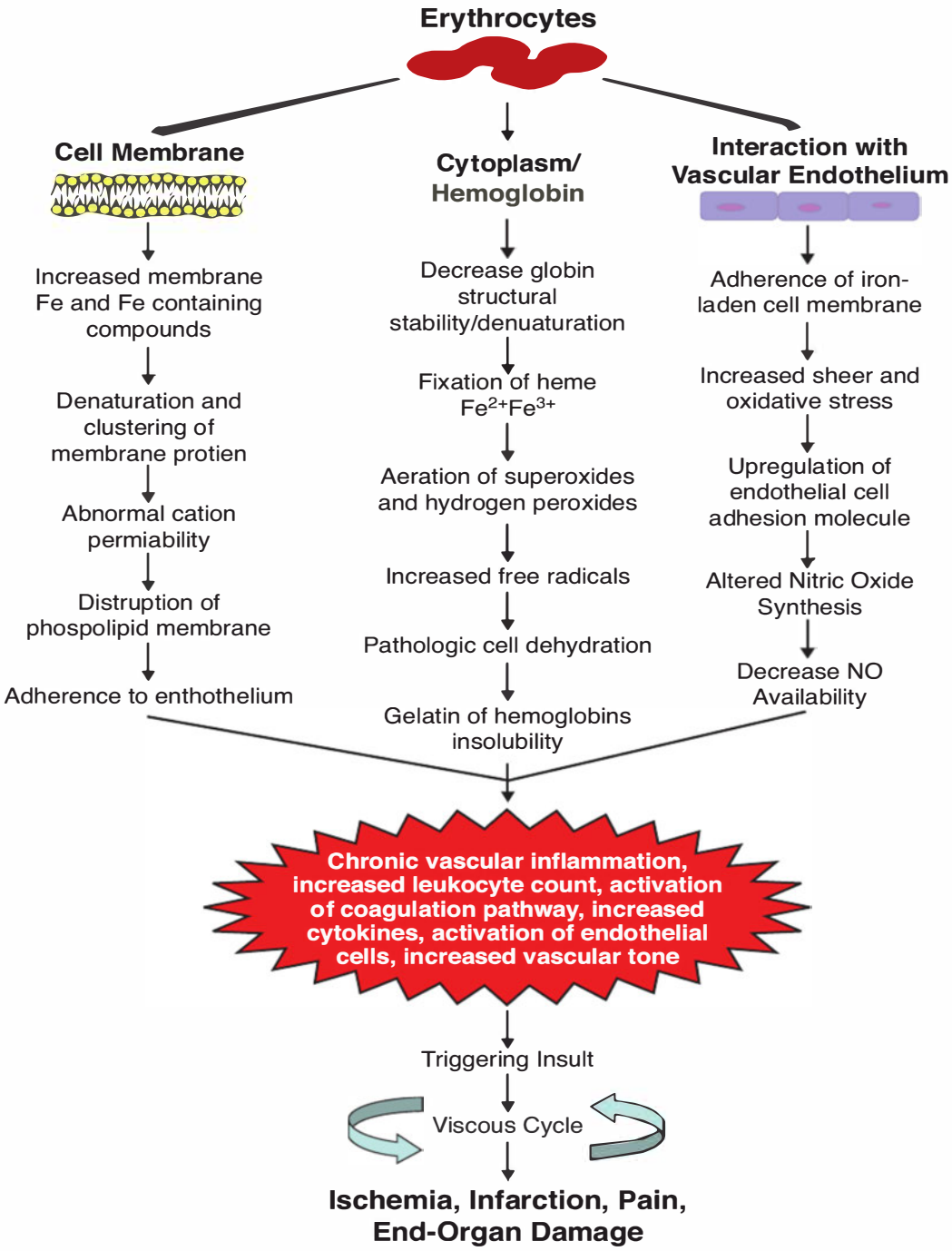

Figure 32.1 Pathogenesis of sickle cell damage.

can be prevented by judicious hydration, incentive spirometry, effective analgesia, and avoidance of even mild hypothermia during the crises. Acute chest syndrome should be treated with bronchodilators, antibiotics, and exchange transfusion, when necessary.

Castro O, Brambilla DJ, Thorington B. The acute chest syndrome in sickle cell disease: incidence and risk factors. *Blood*. 1994;84:643.

Emre U, Miller ST, Gutierez M, et al. Effect of transfusion in acute chest syndrome of sickle cell disease. *J Pediatr*. 1995;125:901–904.

Stuart MJ, Yamaja S. Sickle cell acute chest syndrome: pathogenesis and rationale for treatment. *Blood*. 1999;94:1555.

Vichinsky EP, Haberkern CM, Neumayo L. A comparison of conservative and aggressive transfusion regimens in the perioperative management of sickle cell disease. *N Engl J Med*. 1995;333:206–213.

Vichinsky EP, Neumayr LD. Causes and outcomes of the acute chest syndrome in sickle cell disease. *New Engl J Med*. 2010;342:1855–1865.

B. Preoperative Evaluation and Preparation

B.1. What preoperative evaluation would you perform on this patient before anesthesia?

The aim of the preoperative assessment in a patient with SCD is to determine the perioperative risk of this multisystemic disease and how the end-organ damage will affect the anesthetic management (see Table 32.1). A careful history should be obtained and physical examination done, and the cardiopulmonary status should be thoroughly investigated, in view of the increased incidence of cardiac and pulmonary morbidity in these patients. A history of frequent hospitalizations in the year before surgery significantly increases the likelihood of a vaso-occlusive crisis in the perioperative period. Immunization status for Pneumovax and *Haemophilus influenzae* vaccine should be checked. Other characteristics that increase the perioperative risk are age, pregnancy, and infection. One should correct hypovolemia and treat infection appropriately preoperatively. Laboratory investigation should include a complete blood count, blood urea nitrogen, serum creatinine, urinalysis, electrocardiogram, chest radiograph, pulse oximetry, and liver function tests. In addition, the following tests may be helpful:

- Arterial blood gas, if indicated
- Sickle cell preparation (if diagnosis is unclear)
- Hgb electrophoresis to determine HbS, quantitatively
- Reticulocyte count
- Type and cross (alloimmunization may make this difficult)
- Pulmonary function test (if severe pathology, paroxysmal dyspnea, or history of acute chest syndrome)
- Echocardiogram in patients with history of pulmonary hypertension or cardiomegaly
- Neurologic imaging (if there are psychological or behavioral changes)

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:634–636.

Firth PG. Anaesthesia for peculiar cells: a century of sickle cell disease. *BJA* 2005;95287–299.

Firth PG. Anesthesia and hemoglobinopathies. *Anesthesiol Clin.* 2009;27321–336. doi:10.1016/j.anclin.2009.05.001.

Firth PG, Head A. Sickle cell disease and anesthesia. *Anesthesiology.* 2004;101:766–785.

Park KW. Sickle cell disease and other hemoglobinopathies. *Int Anesthesiol Clin.* 2004;42:77–93.

B.2. How would you prepare this patient for general anesthesia and regional anesthesia?

- Informed consent should be obtained to explain the options, risk, and benefits of the different types of anesthetics used.
- Preoperative hydration should be initiated to treat baseline volume deficit.
- Euvolemia should be maintained preoperatively (remembering that the patient is on nothing by mouth status and may have a urine concentration defect requiring volume replacement).
- Any infections should be treated preoperatively, if possible.
- End-organ dysfunction should be identified and treated appropriately.
- Type and crossmatching may be difficult in these patient's because of alloimmunization.
- Consider transfusion of red blood cells to maintain oxygen-carrying capacity. Transfusion guidelines should be based on comorbidities, surgical risk, and degree of anemia. Transfusions should be individualized and based on the patient's risk/benefit. Efforts should be made for leukocyte reduction techniques, as with buffy coat–poor red cells, to reduce the incidence of leukocyte antigen alloimmunization. The goals of transfusion are to achieve an Hgb concentration of greater than 8 g per dL and to ensure that Hgb A represents more than 40% of the total Hgb present. Past practices of reducing HgbS levels to less than 30% do not seem to improve outcome and increase transfusion-related complications.

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia.* 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:634–636.

Firth PG. Anesthesia and hemoglobinopathies. *Anesthesiol Clin.* 2009;27:321–336. doi:10.1016/j.anclin.2009.05.001.

Firth PG. Anaesthesia for peculiar cells: a century of sickle cell disease. *BJA.* 2005;95:287–299.

Lane PA. Sickle cell disease. *Pediatr Clin North Am.* 1996;43:639–664.

Reed WF, Vichinsky EP. Transfusion practice for patients with sickle cell disease. *Curr Opin Hematol.* 1999;6:432–436.

Schmalzer EA, Lee J, Brown AK, et al. Viscosity of mixtures of sickle and normal cells at varying hematocrit levels: implications for transfusion. *Transfusion.* 1987;27:228–236.

Vichinsky EP, Haberkern CM, Neumayer L, et al. A comparison of conservative and aggressive transfusion regimens in the perioperative management of sickle cell disease. *N Engl J Med.* 1995;333:206–213.

B.3. Discuss the indications for preoperative exchange transfusion in this patient.

Controversy exists as to whether these patients benefit from preoperative exchange transfusion. For high-risk surgical procedures such as cardiopulmonary bypass an exchange transfusion may be recommended. Nevertheless, a series of reports of cardiopulmonary bypass cases in which exchange transfusions were not performed or only a partial exchange was performed. If an exchange transfusion is required, the

exchange transfusion should be performed with buffy coat–free packed red blood cells to reduce the HbS fraction to less than 40%. Nevertheless, growing evidence indicates that most surgical procedures can be safely performed in patients with SCD without aggressively transfusing. For example, for certain surgical procedures, it has been shown that a packed red blood cell transfusion done simply to increase the Hgb level to 10 g per dL is as effective in decreasing perioperative morbidity as is exchange transfusions to reduce the HbS(S) levels to less than 40%. Exchange transfusion is a therapy often used in patients with SCD complicated by acute chest syndrome. It is beneficial to keep the hematocrit lower than 35% with an exchange transfusion because an increased hematocrit will increase blood viscosity and stasis in the circulation.

Adhikari RK, Maddi NM. Preoperative exchange transfusion for sickle cell disease patients undergoing open heart surgery: exception to the rule. *J Cardiac Surg*. 2010;25(6):691–693.

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:634–636.

Koshy M, Weiner SJ, Miller ST, et al. Surgery and anesthesia in sickle cell disease: cooperative study of sickle cell diseases. *Blood*. 1995;86:3676–3684.

Maddoli MM, Rajakumar MC. Cardiopulmonary bypass without preoperative exchange transfusion in sicklers. *Asian Cardiovasc Thorac Ann*. 2006;14:51–56.

Vichinsky EP, Haberkern CM, Neumayo L. A comparison of conservative and aggressive transfusion regimens in the perioperative management of sickle cell disease. *N Engl J Med*. 1995;333:206–213.

B.4. What are the indications for blood transfusion in SCD?

Blood transfusions should be guided by the clinical picture and the potential for blood loss. Prophylactic transfusion remains controversial and is of questionable benefit in mild-to-moderate risk cases. Some of the clinical indications for blood transfusion in SCD include the following:

Acute conditions

- Vaso-occlusive crises with organ infarction and dysfunction
- Sequestration syndrome
- Acute hemolysis with exacerbation of anemia
- Aplastic crisis
- Acute chest syndrome
- Acute multiorgan failure
- Severe unresponsive priapism
- Protracted painful crisis
- High-risk surgery (e.g., cardiovascular, thoracic)

Chronic conditions

- Intractable leg ulcers
- Complicated pregnancy
- Stroke
- Recurrent painful syndrome
- Recurrent acute chest syndrome

Embury SH, Hebbel RP, Mohandas N, eds. *Transfusion Therapy in Sickle Cell Disease: Basic Principles and Clinical Practice*. New York: Raven Press; 1994:781–798.

Reed WF, Vichinsky EP. Transfusion practice for patients with sickle cell disease. *Curr Opin Hematol*. 1999;6:432–436.

C. Intraoperative Management

C.1. Discuss the anesthetic management for this patient. Discuss both regional and general anesthesia considerations.

The definitive anesthetic technique has not been established secondary to the wide clinical spectrum of SCD and the different severities in the surgical procedures. Koshy et al. retrospectively reviewed 1,079 anesthetics and noted an apparent association between postoperative complications and the use of regional anesthesia. Nevertheless, this study did not control for obstetric procedures and the tendency that clinicians often use regional anesthesia for sicker patients. Other studies did not find an adverse effect of regional anesthesia. Theoretically, regional anesthesia, especially when used with epinephrine, may produce a compensatory vasoconstriction in the nonblocked area, but this has not been supported in the literature. Yaster et al. found that epidural analgesia markedly improved oxygenation in children in vaso-occlusive crises, either through superior pain control or opioid sparing effects. Therefore, almost any anesthetic technique can be used, provided the following principles are considered:

- Good intravenous access for maintenance of intravascular volume
- Adequate oxygenation
- Denitrogenation before induction of general anesthesia
- Endotracheal intubation for general anesthesia to ensure a controlled airway and adequate ventilation
- Maintenance of adequate oxygen-carrying capacity through judicious use of red cell transfusions
- Maintenance of normothermia
- Opioids for analgesia carefully titrated for perioperative and postoperative analgesia
- Avoidance of tourniquet use
- Considering regional analgesia for both intraoperative and postoperative courses
- Avoidance of hypotension and venous stasis to prevent sickling of red blood cells
- Considering invasive monitoring (arterial line, central venous pressure line) for beat-to-beat blood pressure monitoring, volume monitoring, and frequent laboratory test
- Avoidance of hypoventilation of lungs to prevent acidosis
- Possible increased inspired oxygen concentration to ensure maintenance of normal to increased Pa_{O_2}

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:634–636.

Firth PG. Anaesthesia for peculiar cells-a century of sickle cell disease. *BJA*. 2005;95:287–299.

Firth PG. Anesthesia and hemoglobinopathies. *Anesthesiol Clin*. 2009;27:321–336. doi:10.1016/j.anclin.2009.05.001.

Garden MS, Grant RE, Jebraili S. Perioperative complications in patients with sickle cell disease. *Am J Orthop*. 1996;25:353–356.

Gregory CGA, ed. *Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 2002:140–142.

Koshy M, Weiner SJ, Miller ST, et al. Surgery and anesthesia in sickle cell disease: cooperative study of sickle cell diseases. *Blood*. 1995;86:3676–3684.

Yaster M, Tobin JR, Billett C, et al. Epidural analgesia in the management of severe vaso-occlusive sickle cell crises. *Pediatrics*. 1994;93:310–315.

C.2. Discuss how the comorbidities associated with SCD can affect your anesthetic management.

Sickle cell anemia is a disease that can affect every end organ. Therefore, evaluating the patient for end-organ dysfunction is paramount. This patient is anemic, tachycardic,

and hypertensive. She may have dyspepsia, a hyperreactive airway, chronic renal insufficiency, liver disease, and might be debilitated with cardiopulmonary complications. Patients with SCD often present with cardiomegaly, pulmonary hypertension, and heart failure. For this surgery, she will probably require transfusions and may be difficult to crossmatch. In the postoperative period, pulmonary infarcts and infection are common, which can lead to acute chest syndrome. These problems, in addition to the potential for sickling crisis or sequestration syndrome, pose a greater risk than normal for perioperative morbidity and mortality. The patients at greater risk include those with a homozygous state SCD, sickle C disease (HbSC), and sickle thalassemia. In contrast, patients with SCT do not present an increased risk for intraoperative morbidity. As a perioperative specialist, one can have a profound effect on outcome in these patients by attention to detail, with a multisystem approach to address all end-organ dysfunction to reduce morbidity by maintaining oxygen delivery and preventing ongoing sickling.

Covitz W, Espeland M, Gallagher D, et al. The heart in sickle cell anemia: the Cooperative Study of Sickle Cell Disease. *Chest* 1995;108:1214–1219.

Firth PG. Anaesthesia for peculiar cells: a century of sickle cell disease. *BJA.* 2005;95:287–299.

Firth PG. Anesthesia and hemoglobinopathies. *Anesthesiol Clin.* 2009;27:321–336.

Gregory GD, ed. *Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 2002: 140–142.

Koshy M, Weiner SJ, Miller ST, et al. Surgery and anesthesia in sickle cell disease: Cooperative Study of Sickle Cell Diseases. *Blood.* 1995;86:3676–3684.

C.3. What precautions should one take to prevent sickling in this patient?

Sickling of red blood cells is triggered by a variety of factors. One should avoid or correct factors that can precipitate sickling. Special precautions include the following:

- Avoid hypoxia by preoxygenating the patient and employing higher than usual concentrations of inspired oxygen.
- Prevent acidosis by maintaining adequate oxygenation, normovolemia, and cardiac output.
- Prevent respiratory acidosis by avoiding hypoventilation.
- Prevent stasis. This requires proper hydration and good regional blood flow. Blood viscosity should be maintained at a low level by limiting a rise in hematocrit to 35% and avoiding over transfusion.
- Avoid hypovolemia.
- Avoid hypothermia by using body warming and intravenous fluid warming devices perioperatively.
- Replace blood loss to prevent anemia.
- The use of tourniquets is controversial. Some advise against the use of tourniquets, although they have been used without ill effects by others. If a tourniquet is to be used, it should only be used when absolutely necessary and for a short period as possible. Special attention should be paid to maintain adequate oxygenation and to prevent respiratory or metabolic acidosis at the time of tourniquet release.

Barash PG, Cullen BF, Stoelting RK, et al. eds. *Clinical Anesthesia.* 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:634–636.

Firth PG. Anaesthesia for peculiar cells-a century of sickle cell disease. *BJA.* 2005;95:287–299.

Firth PG. Anesthesia and hemoglobinopathies. *Anesthesiol Clin.* 2009;27:321–336.

Gregory GD, ed. *Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 2002:140–142.

Oginni LM, Rufai MB. How safe is tourniquet use in sickle-cell disease? *Afr J Med Med Sci.* 1996;25:3–6.

D. Postoperative Management

D.1. Discuss the postoperative management of this patient.

The postoperative period is a crucial time with SCD. Surgical pain, hypoventilation, a high incidence of pulmonary infarction, and an expected decrease in Pao_2 will predispose these patients to the formation of sickle cells, leading to the possibility of developing vaso-occlusive crisis or acute chest syndrome. The mainstay of postoperative management is supportive and preventive care. Supplemental oxygen, maintenance of intravascular fluid volume, maintenance of normothermia, and adequate analgesia are important considerations. Regional analgesia has been shown to decrease pain scores while improving oxygenation. Supportive and preventive care should be continued in the extended postoperative period. The basic outline of routine postoperative care includes the following:

- Early mobilization
- Maintenance of normothermia
- Supplemental oxygenation
- Early effective analgesia or adjunctive analgesics—nonsteroidal anti-inflammatory drugs, acetaminophen
- Maintain euvolemia
- Incentive spirometry
- Pulse oximetry
- Pulmonary monitoring
- Psychological support
- Considering extended postoperative cardiovascular monitoring
- Considering regional analgesia for postoperative pain management

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*.6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:634–636.

Firth PG. Anaesthesia for peculiar cells-a century of sickle cell disease. *BJA*. 2005;95:287–299.

Firth PG. Anesthesia and hemoglobinopathies. *Anesthesiol Clin.* 2009;27:321–336.

Gregory GD, ed. *Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 2002:140–142.

Park KW. Sickle cell disease and other hemoglobinopathies. *Int Anesthesiol Clin.* 2004;42:77–93.

Yaster M, Tobin JR, Billett C, et al. Epidural analgesia in the management of severe vaso-occlusive sickle cell crises. *Pediatrics*. 1994;93:310–315.

D.2. What complications might occur in this patient in the immediate postoperative period?

The postoperative complications most likely to occur in the patient with SCD include deep vein thrombosis, vaso-occlusive crisis, pulmonary infarction, acute chest syndrome, and infection. Hypoxemic episodes are always a threat in the postoperative period secondary to pain, splinting, or oversedation and can precipitate a sickling crisis. The incidence of postoperative respiratory infection is high and is a leading

cause of morbidity and mortality. Acute chest syndrome is one of the most common causes of death in adult patients and is a potentially lethal postoperative complication in patients with SCD who undergo major or high-risk surgery. Sequestration syndrome with shock is another potentially lethal complication, especially in the obstetric patient immediately postpartum. Patients with cardiomegaly and pulmonary hypertension are susceptible to heart failure. Renal and hepatic dysfunction may result in prolongation of the effects of certain medications. Orthopedic patients with SCD are at risk for deep vein thrombosis, acute thrombosis, and pulmonary embolism. Antithrombotic therapy has to be geared toward decreasing this common complication.

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:634–636.

Firth PG. Anaesthesia for peculiar cells: a century of sickle cell disease. *BJA*. 2005;95: 287–299.

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Vichinsky EP, Haberkern CM, Neumayo L. A comparison of conservative and aggressive transfusion regimens in the perioperative management of sickle cell disease. *N Engl J Med*. 1995;333:206–213.

D.3. What is the treatment of sickle cell crisis?

The treatment of sickle cell crisis is to break the vicious cycle of sickling, ischemia, infarction, pain, and end-organ failure. The principles of treatment of painful sickle cell crisis include the following:

- Rest
- Hydration
- Oxygen therapy
- Treatment of infection
- Analgesics (consider patient-controlled analgesia)
- Considering regional analgesia
- Transfusion to reduce the Hgb SS disease concentration
- Incentive spirometry
- Maintenance of normothermia

Barash PG, Cullen BF, Stoelting RK, et al. eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:634–636.

Firth PG. Anesthesia and hemoglobinopathies. *Anesthesiol Clin*. 2009;27:321–336.

Steinberg MH. Management of sickle cell disease. *N Engl J Med*. 1999;340:1021–1030.

Vijay V, Cavenagh JD, Yate P. The Anaesthetist's role in acute sickle cell crisis. *Br J Anaesth*. 1998;80:820–828.

D.4. What is the role of hyperbaric oxygen therapy in treatment of sickle cell crisis?

Hyperbaric oxygen has been used empirically in some institutions for treatment of acute sickle cell crisis, though it is not widely available. Although some published reports claim instant improvement of symptoms, others have failed to show beneficial effects. There is better evidence that therapy is useful in management of ischemic

disorders of the anterior segment of the eye or in chronic leg ulcers. Studies have shown no apparent effects of hyperbaric oxygen on sickle cell morphology in vitro. It appears, then, that its reported benefit in vivo may be due to a decrease in the rate of sickling or improved tissue oxygenation by direct diffusion.

Butler FK Jr, Hagan C. Hyperbaric oxygen therapy and the eye. *Undersea Hyperaric Med* 2008;35:331–332.

Mychaskiw G, Woodyard SA, Brunson CD, et al. In vitro effects of hyperbaric oxygen on sickle cell morphology. *J Clin Anesth.* 2001;13:255–258.

Reynolds JD. Painful sickle cell crisis: successful treatment with hyperbaric oxygen therapy. *JAMA.* 1971;216:1977–1978.

Wallyn CR, Jampl LM, Goldberg MF, et al. The use of hyperbaric oxygen in treatment of sickle cell hyphema. *Invest Ophthalmol Vis Sci.* 1985;26:1155–1158.

SECTION IX

Eye, Ear, Nose, and Throat

CHAPTER 33

Airway Trauma

Richard P. Dutton and LaRita Yvette Fouchè-Weber

A 46-YEAR-OLD MAN

was thrown from his motorcycle at a high rate of speed and impaled in the base of the neck by a tree branch. At presentation to the trauma center, he is awake and alert with heart rate (HR) of 122 beats per minute, blood pressure (BP) of 143/85 mm Hg, respiratory rate of 20 per minute, and oxygen saturation of 98% on 100% nonrebreathing mask. There is a 5-cm wide piece of wood protruding from his anterior lower neck at the sternal notch, without visible bleeding. The patient is neurologically intact but admits to consuming six beers in the hours before injury. His medical history is unremarkable.

A. Medical Disease and Differential Diagnosis

1. What variables mitigate injury from motorcycle collisions?
2. What other significant trauma may be present?
3. How is the initial assessment of a trauma patient organized?
4. How would you evaluate airway and breathing?
5. How would you evaluate the circulation?
6. How would you evaluate mental status and neurologic condition?
7. What diagnostic tests are indicated for this patient based on the mechanism of injury?
8. What are the zones of the neck and what is their clinical significance?
9. What immediate treatment is necessary before diagnostic studies?
10. When and where should the impaling object be removed?

B. Preoperative Evaluation and Preparation

1. What laboratory tests would you want?
2. What x-ray studies are most important to the anesthesiologist?
3. Is an electrocardiogram (ECG) necessary?
4. Should this patient be intubated before going for computed tomographic (CT) scanning?
5. When and where should this patient's airway be managed?
6. Are any prophylactic medications indicated?

C. Intraoperative Management

1. What monitors would you use? Is invasive monitoring necessary before definitive airway control?
2. What is the surgical approach to a zone I neck injury?
3. Is the patient likely to require tube thoracostomy? Should this be placed before managing the airway?
4. What are the options for managing this patient's airway?
5. What are the risks of rapid-sequence induction in this patient?
6. What anesthetic agents would you use for a rapid-sequence induction?
7. How can you minimize the risk of exacerbating cervical spine trauma?
8. How can you minimize the risks of aspiration?
9. How would you anesthetize the airway for an awake intubation?
10. What are the risks of awake fiberoptic intubation?
11. If the patient cannot be ventilated, what options are available?
12. Would a laryngeal mask airway (LMA) or other pharyngeal airway be of assistance?
13. What surgical airway options are available in this case?
14. What maintenance anesthetics are indicated or contraindicated in this patient?
15. What complications will the surgical plan introduce?

D. Postoperative Management

1. What are the criteria for extubation?
2. What techniques may be used during extubation?
3. How does alcohol abuse affect postoperative management?
4. What pain medication should be used?

A. Medical Disease and Differential Diagnosis

A.1. What variables mitigate injury from motorcycle collisions?

Trauma involving motorcycles accounts for 2% to 5% of all motor vehicle trauma, but a higher proportion of death and serious injury because of the relative exposure of the motorcycle rider to the environment. Factors such as youth, high speed, and intoxication contribute to motorcycle collisions just as they do for automobiles. Motorcycle riders also are much more susceptible to factors beyond their own control, such as lack of vigilance on the part of automobile and truck drivers, road conditions (oil or debris), and the weather.

Factors that can reduce the seriousness of motorcycle collisions when they do occur include helmets and protective clothing. Reenactment of a mandatory helmet law in the state of Washington in 1990 resulted in a decline in serious brain injury in motorcycle trauma victims from 20% to 9%, and a reduction in mortality from 10% to

6%. Full leather or synthetic "armor" reduces the risk of massive skin and soft-tissue injuries in the event of a high-speed collision.

Mock CN, Maier RV, Boyle E, et al. Injury prevention strategies to promote helmet use decrease severe head injury at a level I trauma center. *J Trauma*. 1995;39:29.

A.2. What other significant trauma may be present?

Motorcycle collisions are "high-energy" trauma that can result in injury to any organ system or region of the body. This patient will need a complete head-to-toe assessment and a number of diagnostic studies to establish the full extent of injury. Common injuries in motorcyclists include brain trauma from direct impact with the road and with other vehicles, pelvic fractures from impact with the frame of the motorcycle, abdominal trauma from impact with the handlebars, and lower extremity orthopedic and soft-tissue trauma from impact with the road.

A.3. How is the initial assessment of a trauma patient organized?

The initial management of trauma patients is best described by the tenets of the Advanced Trauma Life Support course, written by the American College of Surgeons Committee on Trauma. This course provides a unified philosophy and common language to organize practitioners from different specialties in the care of complex patients with the potential for multiple injuries. Assessment of the seriously injured patient begins with the ABCs: *A*irway, *B*reathing, and *C*irculation; followed by a brief neurologic examination and a catalogue of visible injuries. This "primary survey" is followed by diagnostic testing and a more detailed secondary survey to discover all of the patient's injuries. One important principle of Advanced Trauma Life Support is interruption of the diagnostic sequence as necessary to provide life-saving resuscitative care, up to and including surgery for airway management or hemorrhage control prior to completion of diagnostic studies.

Committee on Trauma, American College of Surgeons. *Advanced Trauma Life Support for Doctors*. 8th ed. Chicago: American College of Surgeons; 2008.

A.4. How would you evaluate airway and breathing?

On first contact with the patient, the provider should attempt verbal communication: "How are you?" A patient who answers coherently in a normal voice has no immediate airway issue, adequate circulatory function, and minimal traumatic brain injury. In an unconscious patient, initial assessment is by looking, listening, and feeling for airflow. If airflow is absent, the airway should be opened by jaw thrust (*not* head tilt, as this may exacerbate a cervical spinal column injury), clearance of any visible foreign bodies or secretions, and placement of an oral or nasopharyngeal airway.

Breathing is assessed by observation of the chest wall and diaphragm once the airway is open, and by immediate placement of a pulse oximeter probe. Patients who are not breathing adequately should be assisted with bag-valve-mask ventilation while preparations are made for securing a definitive airway and instituting mechanical ventilation.

A.5. How would you evaluate the circulation?

Initial assessment for shock is by vital signs (HR, blood pressure, pulse oximetry) and physical examination (pallor, diaphoresis, peripheral circulation, visible or suspected hemorrhage). Mental status is also a useful sign: The patient in hemorrhagic shock will be first agitated and then lethargic. Young patients have significant compensatory

reserves and will maintain a normal systolic blood pressure even in the face of hemorrhage as great as 40% of the blood volume. This state of compensated shock can be diagnosed by a narrowed pulse pressure (especially on automated sphygmomanometers), elevated HR, pallor, and abnormal lactate and base deficit. Shock in this patient could be the result of hemorrhage from chest or abdominal trauma (including a great vessel injury associated with the impalement) or tension pneumothorax in either side of the chest.

Committee on Trauma, American College of Surgeons. *Advanced Trauma Life Support for Doctors*. 8th ed. Chicago: American College of Surgeons; 2008.

Dutton RP. Initial resuscitation of the hemorrhaging patient. In: Speiss B, Shander A, eds. *Perioperative Transfusion Medicine*. Philadelphia: Lippincott Williams & Wilkins; 2006:289–300.

A.6. How would you evaluate mental status and neurologic condition?

The quick neurologic examination consists of questions to determine alertness and orientation (assuming the patient is responsive) followed by gross assessment of voluntary motion in all extremities. In the less responsive patient, the Glasgow Coma Score (GCS) (Table 33.1) is used to stratify the degree of impairment: GCS 3 to 8 is a severe injury, GCS 9 to 13 is moderate traumatic brain injury, and GCS 14 to 15 is mild injury. Cranial nerve, spinal cord, and peripheral nervous system function is assessed by specific motor and sensory testing of each extremity during the secondary survey.

Teasdale G, Jennet B. Assessment of coma and impaired consciousness: a practical scale. *Lancet*. 1974;2:81–84.

A.7. What diagnostic tests are indicated for this patient based on the mechanism of injury?

Because of the "high energy" mechanism of injury, this patient must be assessed from head to toe. Ultrasonography examination of the abdomen and chest is used to diagnosis free peritoneal fluid, pneumothorax (in the hands of a skilled operator), and pericardial tamponade. Chest and pelvis plain-film radiography will reveal fractures, pneumothoraces, and hemothorax. CT scanning should include the head, neck, chest,

Table 33.1 Glasgow Coma Scores[a]

EYE-OPENING RESPONSE	VERBAL RESPONSE	MOTOR RESPONSE
4 = Spontaneous	5 = Oriented to name	6 = Follows commands
3 = To speech	4 = Confused	5 = Localizes to painful stimuli
2 = To pain	3 = Inappropriate speech	4 = Withdraws from painful stimuli
1 = None	2 = Incomprehensible sounds	3 = Abnormal flexion (decorticate posturing)
	1 = None	2 = Abnormal extension (decerebrate posturing)
		1 = None

[a]The GCS is the sum of the best scores in each of three categories.

abdomen, and pelvis; newer technology will allow for 3D reconstructions of organs and vasculature with sensitivity and specificity equivalent to more traditional angiographic imaging.

This patient's obvious injury—to zone I of the neck—will necessitate a focused assessment of the trachea, great vessels, esophagus, and bilateral pleural cavities. Traditionally, this has been accomplished by a combination of plain-film radiography, angiography, bronchoscopy, and esophagoscopy. Increasing CT speed and resolution is leading to the increased use of this test at centers with experienced radiographers and traumatologists. The sequencing of diagnostic studies will depend on the patient's stability. In this case, he is likely to require intubation and perhaps exploratory surgery first. A noninvasive study such as contrast-enhanced CT (with angiographic reconstructions) may help to guide the surgical approach to removal of the impaling object if the patient is calm and stable enough to tolerate the test.

Henry SM, Scalea TM. Assessment and initial management in the trauma patient. In: Prough DS, Fleisher L, eds. *Prob Anesth Trauma Care.* Vol. 13, no. 3. London: Lippincott Wiliams & Wilkins; 2002:271–278.

A.8. What are the zones of the neck and what is their clinical significance?

Zone I of the neck includes the area from the inferior aspect of the cricoid cartilage down to the thoracic outlet. Zone I injuries require the complex diagnostic workup described in the previous section, followed by a surgical approach that allows access to both the neck and chest. Partial or complete median sternotomy is often necessary to access an injured great vessel or to repair the trachea or esophagus.

Zone II of the neck includes the area from the angle of the mandible down to the cricoid cartilage. Injuries in zone II are addressed through a lateral or transverse cervical incision, with the surgeon able to achieve both proximal and distal control of the carotid or jugular vessels before exploring the wound itself.

Zone III of the neck includes the area from the angle of the mandible upward to the base of the skull. Zone III vascular injuries pose a significant operative risk because distal control of an injured vessel cannot be achieved. Injuries in zone III are therefore approached angiographically or as part of a more complex neurosurgical operation.

Britt LD, Weireter LJ, Cole FJ. Management of acute neck injuries. In: Feliciano DV, Mattox KL, Moore EE, eds. *Trauma.* 6th ed. New York: McGraw-Hill; 2008:467–478.

A.9. What immediate treatment is necessary before diagnostic studies?

The key to this case will be control of the patient's airway. Once hemodynamic stability is confirmed, the timing and sequence of diagnostic studies will be determined by the patient's degree of cooperation and ability to protect his own spontaneous ventilation. Although a CT scan before a controlled intubation in the operating room (OR) would be ideal, it is possible that the patient will decompensate before this can be accomplished. Preemptive airway control will allow for a more secure and safer diagnostic workup before the OR.

A.10. When and where should the impaling object be removed?

All things being equal, the impaling tree branch is best removed in the OR in an anesthetized patient, with all of the personnel and equipment on hand to perform emergent median sternotomy and major vascular and/or tracheal surgery if necessary.

B. Preoperative Evaluation and Preparation

B.1. What laboratory tests would you want?

The patient should have a full set of laboratory studies, both to identify abnormalities and to establish a baseline for future changes. Hemoglobin and hematocrit will not indicate hemorrhage on the initial draw—the bleeding trauma patient is losing whole blood—but will drop with subsequent fluid resuscitation. Arterial blood gas and arterial or venous lactate measurement will be the most sensitive indicators of hypoperfusion and shock. Serum electrolytes will reveal baseline abnormalities, if any, and the effects of alcohol consumption and dehydration. Clotting studies are important to rule out congenital abnormalities or the effects of liver disease before what could be a major surgical procedure; coagulopathy at the time of trauma center admission is an indicator of substantial blood loss and severe hemorrhagic shock. Toxicology screening is indicated in every trauma patient and is important to rule out the use of drugs of abuse such as heroin or cocaine that have implications for the anesthesiologist.

Initial laboratory studies also should include a sample for the blood bank with the request for an urgent crossmatch of red cells and plasma. If there has been a major vascular injury, substantial blood loss is a possibility and should be treated with immediate transfusion of blood and coagulation factors.

Committee on Trauma, American College of Surgeons. *Advanced Trauma Life Support for Doctors*. 8th ed. Chicago: American College of Surgeons; 2008.

Hess JR, Lindell AL, Stansbury LG, et al. The prevalence of abnormal results of conventional coagulation tests on admission to a trauma center. *Transfusion*. 2009;49(1):34–39.

B.2. What x-ray studies are most important to the anesthesiologist?

Although all of the studies described in the preceding text will have some relevance, there are a few that have particular implications for the anesthesiologist. The chest radiograph and/or CT scan will suggest the degree of tracheal involvement of the impaling object, the risk that there is a major vascular injury, or the presence of a pneumothorax. Plain radiographs or CT scan of the cervical spine will be useful in ruling out bony or ligamentous injury that might be exacerbated by manipulation of the neck during airway management.

B.3. Is an electrocardiogram (ECG) necessary?

In the absence of dysrhythmias on the cardiac monitor, the criteria for ordering a preoperative ECG are the same as in any other surgical candidate: Patients presenting with symptoms or with a history suggestive of coronary artery disease. Dysrhythmias or visible injury to the precordium would be an indication for a baseline ECG and cardiac enzyme assay.

B.4. Should this patient be intubated before going for computed tomographic (CT) scanning?

The answer to this question involves an assessment of risks and benefits. If the patient is cooperative, vital signs are stable, CT scanner is close at hand, and anesthesia personnel are available to accompany the patient, then an immediate CT scan would be indicated. If the patient is deteriorating in any way, his degree of cooperation is in doubt, or a CT scan would place the patient far from expert resources for an extended period of time, then it would be wise to secure the airway first. In this case, there is a possibility that successful airway management will precipitate patient deterioration (e.g., hemorrhage, conversion from simple to tension pneumothorax), which suggests

that if airway management is attempted before CT, it should probably be done in the OR with the surgical team on hand.

One approach to this kind of complex decision is to define an ideal course of care that provides the best information for each of the experts involved while minimizing risk to the patient and maximizing flexibility in dealing with changing circumstances. In this case, the surgeon and anesthesiologist might define a plan that includes transport to the OR; induction, intubation, and mechanical ventilation in this (safest possible) environment; transport to CT or angiography with the anesthesiologist in attendance for diagnostic studies; then return to the OR for definitive surgery.

B.5. When and where should this patient's airway be managed?

Because of the potential for rapid deterioration and the desire to examine the airway closely before and during the intubation process, the patient should be moved as rapidly as possible to the OR before airway management is attempted. The surgical team should be on hand from the start and instruments should be available for video laryngoscopy and bronchoscopy, emergent tracheostomy, control of large vessel bleeding, and median sternotomy.

B.6. Are any prophylactic medications indicated?

Tetanus toxoid treatment is indicated for any trauma patient with an open wound who is more than 5 years removed from his or her last booster. Any patient with a significant open wound should receive prophylactic antibiotic therapy that covers gram-positive organisms for at least the first 24 hours following injury.

Prophylactic treatment to reduce the consequences of aspiration would be considered, but probably rejected in this case. Promotility agents such as metaclopramide and H_2 antagonists such as ranitidine will not have time to work before definitive airway control is achieved and the more immediate approach of administering oral bicitrate would be contraindicated because of the possibility of esophageal injury.

Because of the patient's history of intoxication, prophylactic intravenous administration of vitamins and thiamine is indicated. Prophylaxis against alcohol withdrawal and deep venous thrombosis are indicated in the immediate postoperative period.

C. Intraoperative Management

C.1. What monitors would you use? Is invasive monitoring necessary before definitive airway control?

Blood pressure, electrocardiography, capnography, and pulse oximetry should be employed as with any patient. A Foley catheter should be inserted once the patient is anesthetized, although urine output is not an accurate measure of intravascular volume status in a recently intoxicated patient. An arterial line is useful for moment-to-moment measurement of blood pressure and for easy access to blood for laboratory assay including arterial blood gases. A central venous catheter should be placed if there is need to monitor central venous intravascular volume, in anticipation of the need for rapid intravascular expansion (using a large-bore catheter such as a pulmonary artery introducer), and for the administration of vasoactive drugs. A pulmonary artery catheter is rarely indicated and seldom used acutely for resuscitation, although it may be helpful in selected patients with known coronary artery or valvular disease. Because of the potential for great vessel injury in this case, initial central access should be through the femoral vein.

Invasive monitoring lines usually are best placed after induction and intubation, when the patient is anesthetized and both surgeons and anesthesiologists can be working at the same time. Delaying surgical hemostasis in an unstable patient is

unwise. In the case under discussion, it would be appropriate to place an arterial line in the OR before airway management, as long as the patient remains cooperative and stable, and to place a femoral central line thereafter. Placing the arterial line on the right side also will allow for assessment of blood flow in the innominate artery during surgical exploration.

Dutton RP, McCunn M, Grissom TE. Anesthesia for trauma. In Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier Churchill Livingstone; 2010:2277–2311.

C.2. What is the surgical approach to a zone I neck injury?

In the present case, the surgery is likely to start with a collar incision through the impalement wound to allow for better visualization of the path of injury. If injury to the trachea or a great vessel is discovered, a partial or complete median sternotomy would be the next step. It is the uncertain nature of this patient's injuries that makes preoperative diagnostic information so valuable, which is why a CT scan before definitive surgery (but after airway management) is a strong consideration.

C.3. Is the patient likely to require tube thoracostomy? Should this be placed before managing the airway?

Pneumothorax and hemothorax are common in trauma patients and should be suspected and definitively ruled out following any "high energy" blunt trauma (motor vehicle collision, pedestrian struck, fall from a height) or any penetrating trauma to the neck, thorax, or upper abdomen. Immediate temporizing needle decompression and/or tube thoracostomy are indicated in any hemodynamically unstable patient with a suspicious injury, even before chest radiograph. Intubation and the change to positive pressure ventilation may precipitate decompensation in a patient with chest injury, due to either decreased preload in the setting of hemorrhage or increased intrathoracic pressure caused by conversion from simple to tension pneumothorax.

In this case, there is the possibility of pathology in either or both hemithoraces. A portable anterior–posterior chest radiograph should be obtained at the earliest moment, followed by CT of the chest as outlined previously. If a simple pneumothorax is present, it is most prudent to prepare for chest tube placement (personnel, equipment) before airway management but to wait until the airway is secure before actually placing the chest tube.

C.4. What are the options for managing this patient's airway?

Choices for induction of anesthesia should be considered in concert with choices for securing the airway and transitioning to positive pressure ventilation. Airway management can occur with the patient awake under topical anesthesia or asleep, with either continued spontaneous ventilation (a "breathe down" induction with a volatile anesthetic) or an immediate transition to positive pressure, as in a rapid-sequence induction.

C.5. What are the risks of rapid-sequence induction in this patient?

Although most trauma patients are best managed with rapid-sequence induction and intubation, this case may represent an exception. Swelling or bleeding in the airway may make intubation physically difficult and the impaling object itself may prevent distal passage of an endotracheal tube. Further, dislodgement due to patient agitation or intubation attempts could precipitate hemorrhage or airway disruption. Finally,

the transition from spontaneous to positive pressure ventilation could precipitate a tension pneumothorax.

Stephens CT, Kahntroff S, Dutton RP. The success of emergency endotracheal intubation in trauma patients: a 10-year experience at a major adult trauma referral center. *Anesth Analg*. 2009;109:866–872.

C.6. What anesthetic agents would you use for a rapid-sequence induction?

Succinylcholine is the key component of a rapid-sequence intubation (RSI). No other relaxant provides as consistently good intubating conditions as quickly and as reversibly as succinylcholine. The usual dose for a trauma patient is 1.5 mg per kg—somewhat greater than normal to compensate for a potentially lower cardiac output due to hemorrhage.

Because succinylcholine has no amnestic or analgesic properties, an induction sedative is also indicated in most patients. Any induction agent, including ketamine or etomidate, will precipitate hypotension in the hypovolemic patient with a high endogenous catecholamine level, so care with dosing is required. In young and previously healthy patients, sodium thiopental in a titrated dose from 1 to 5 mg per kg or propofol 0.5 to 2 mg per kg are effective and inexpensive. Etomidate (0.1 to 0.4 mg per kg) is a reasonable choice in elderly patients or in those with known cardiovascular disease.

Dutton RP, McCunn M, Grissom TE. Anesthesia for trauma. In Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier Churchill Livingstone; 2010:2277–2311.

C.7. How can you minimize the risk of exacerbating cervical spine trauma?

Appropriate precautions must be taken to avoid worsening an occult spinal cord injury. In the worst case, fractures or ligamentous injury can leave the cervical spine so unstable that the normal manipulation of a direct laryngoscopy will injure the spinal cord. This is a low probability event but is of concern to the healthcare team because quadriplegia is a catastrophic complication.

Manual in-line cervical stabilization has been shown to be safe and effective in protecting the cervical spine over tens of thousands of direct laryngoscopies and is the common approach to urgent intubations in the trauma population. Another option commonly used only in patients with known cervical instability is an awake intubation over a fiberoptic bronchoscope. This approach allows for the least manipulation of the neck but requires a cooperative patient who can tolerate the time required for topical anesthesia of the airway and a slower intubation. Awake fiberoptic intubation also may increase the risk of aspiration in patients with a full stomach, especially if topical anesthesia of the pharynx and vocal cords is provided.

Other intubation devices may also decrease the need for manipulation of the neck. Good results have been achieved with the newer generation of video laryngoscopes, lighted stylet intubations, and use of an intubating stylet with a less forceful laryngoscopy. Manual cervical stabilization is recommended with each of these approaches. In a difficult case such as the present one, the intubation technique chosen should be one that the anesthesiologist is experienced and comfortable with; this factor may be more relevant than the specific technology used.

Dutton RP, McCunn M, Grissom TE. Anesthesia for trauma. In Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier Churchill Livingstone; 2010:2277–2311.

Karlin A. Airway management of trauma victims. *Prob Anesth Trauma Care*. 2002;13(3): 279–288.

C.8. How can you minimize the risks of aspiration?

Because any significant injury is associated with decreased gastrointestinal motility, all trauma patients are considered to have full stomachs. The risk of aspiration is further increased by intoxication with drugs or alcohol, obesity, the use of analgesics, and injuries to the face, neck, or abdomen that may lead to bleeding within the gastrointestinal tract.

Minimization of risk is a function of how quickly the intubation must be accomplished. One component of prophylaxis is the normal use of rapid-sequence induction to minimize the time during which the airway is at risk. Another is the use of cricoid pressure (the Sellick maneuver) to obstruct the upper esophagus against passive reflux. Although recent magnetic resonance imaging research has shown significant variability in the relative anatomy of the cricoid ring and the esophagus, casting doubt on the efficacy of cricoid pressure, there is no reason not to do it in most cases. In the case under consideration, there would be a risk of dislodging the impaling object, making cricoid pressure inadvisable. It would be reasonable to administer an H_2 antagonist such as cimetidine and a promotility agent such as metaclopramide if time allowed, but these agents would require 1 to 2 hours to have any substantial effect. An oral antacid is contraindicated because of the potential injury to the esophagus.

Smith KJ, Dobranowski J, Yip G, et al. Cricoid pressure displaces the esophagus: an observational study using magnetic resonance imaging. *Anesthesiology.* 2003;99(1):60–64.

C.9. How would you anesthetize the airway for an awake intubation?

Innervation of the airway can be separated into three neural pathways. If nasal intubation is planned, some method of anesthetizing maxillary branches from the trigeminal nerve is required. Involvement of the posterior tongue will require blockade of the glossopharyngeal nerve. Structures more distal in the airway to the epiglottis will require blockade of vagal branches, with the superior laryngeal nerve supplying the pharyngeal apparatus and the recurrent laryngeal nerve supplying the vocal cord and the tracheal mucosa.

The trigeminal nerve, which supplies sensory innervation to the nasal mucosa, can be anesthetized by inserting a nasal airway lubricated with lidocaine jelly into the patent naris. Mixing the lidocaine jelly with oxymetazoline 0.05%, phenylephrine 10 mg, or 4% cocaine may help vasoconstrict the nasal blood vessels and diminish bleeding from the nasal mucosa. The liquid local anesthetic and vasoconstrictor may also be applied in droplet form from a syringe.

The glossopharyngeal nerves of interest are the tonsillar nerves, which provide sensation to the mucosa overlying the palatine tonsil and continuous parts of the soft palate, and the sensory branches to the posterior one-third of the tongue. First, one must provide topical intraoral anesthesia with local anesthetic spray or nebulized lidocaine. Following topical anesthesia of the tongue, the mouth is opened wide and the posterior tonsillar pillar (palatopharyngeal fold) is identified. Then, a 22-gauge needle can be inserted at the caudad portion of the tonsillar pillar. The needle tip is inserted submucosally and following careful aspiration for blood, 5 mL of 0.5% lidocaine is injected. The block is then repeated on the contralateral side. A similar block can be performed with direct application of anesthetic soaked cotton to the bilateral tonsillar fossae.

The vagus nerve supplies innervation to the mucosa of the airway from the level of the epiglottis to the distal airways through both the superior and recurrent laryngeal nerves. A superior laryngeal nerve block and a translaryngeal block can be useful in anesthetizing these pathways. With the patient lying supine, a 22-gauge needle attached to a syringe is directed at the most posterior palpable part of the hyoid bone, near the greater cornu, and anterior to the carotid sheath. The needle must be parallel

to the table and never directed posteriorly for fear of penetrating the carotid sheath. When the needle strikes the hyoid, it is carefully walked caudad until it just slips off the hyoid, and then advanced a short distance through the hyothyroid membrane. Aspiration should produce nothing. Then 2 mL of 2% lidocaine is injected and the block repeated on the opposite side.

The translaryngeal block is performed with a 20- or 22-gauge needle attached to a syringe. The needle is inserted through the cricothyroid membrane in the midline and air is aspirated. The patient is asked to inhale deeply and then to exhale fully. At the end of expiration, 4 mL of 2% to 4% lidocaine is injected rapidly and the needle is quickly removed. The resultant coughing will ensure a wide distribution of local anesthetic droplets throughout the airway. If stability of the cervical spine is in doubt, then in-line stabilization should be held while the block is performed and coughing occurs. In the present case, both superior laryngeal and transtracheal blocks would be difficult to perform, and induced coughing might exacerbate the injury. Administration of nebulized lidocaine might be a safer choice.

Brown DL. *Atlas of Regional Anesthesia.* 4th ed. Philadelphia: WB Saunders; 2010:191–196.

Gotta AW, Sullivan CA. Anesthesia of the upper airway using topical anesthetic and laryngeal nerve block. *Br J Anaesth.* 1981;53:1055–1058.

C.10. What are the risks of awake fiberoptic intubation?

The greatest risk of awake fiberoptic intubation is deterioration of the patient's airway or mental status (or both) during the procedure. Ineffective topical anesthesia can lead to agitation and combativeness, which in turn leads to increased use of intravenous sedatives. Blood and secretions in the airway can cause coughing, laryngospasm, or aspiration. Oversedation causes respiratory depression and desaturation, which can pressure the anesthesia providers and lead to hasty decisions. More uncommon complications include injury to nerves or vessels during local nerve blocks, toxicity from local anesthesia ingestion, and direct injury to the laryngeal or pharyngeal mucosa.

This particular case also includes the possibility of inadvertent dislodgement of the impaling tree branch during sedation and topicalization or during the intubation effort itself. Bleeding from a loss of tamponade or open disruption of the airway could necessitate a sudden change in anesthetic and surgical plans. Although awake fiberoptic intubation in the OR is a reasonable starting point for this case, the anesthesiologists and surgeons involved must be prepared for other eventualities. These would include both RSI and emergency surgical airway access.

C.11. If the patient cannot be ventilated, what options are available?

Failure of awake fiberoptic intubation in this case should be followed by an immediate attempt at RSI. If RSI is not possible and the patient cannot be ventilated by mask or laryngeal mask airway (LMA), then a surgical airway may be required. An alternate technique involves placing a 14-gauge catheter over a needle through the cricothyroid membrane, removing the needle and using the catheter for jet ventilation. This technique provides a temporary route for oxygenation, as a bridge to a surgical airway, but is highly tenuous. Kinking or dislodgement of the jet catheter are common complications, with tension pneumothorax a possibility if the catheter tip is displaced into the paratracheal tissues. In this case, accessibility to the trachea or cricoid cartilage may be difficult due to the impaling object.

Benumof JL, Scheller MS. The importance of transtracheal jet ventilation in the management of the difficult airway. *Anesthesiology.* 1989;71:769–778.

C.12. Would a laryngeal mask airway (LMA) or other pharyngeal airway be of assistance?

Although an LMA or other supraglottic airway support device is often a great help in the difficult airway algorithm, this case may represent an exception. Establishing an efficient mask airway is beneficial if the cause of patient distress is neurologic (diminished respiratory drive due to anesthesia or traumatic brain injury) or related to pharyngeal anatomy (obstruction after muscle relaxation). Supraglottic ventilation will not help with more distal causes of airway obstruction, such as laryngospasm, tracheal disruption, or massive aspiration. Although an LMA or equivalent device should be on hand when this patient is brought to the OR, it is less likely to be of use.

C.13. What surgical airway options are available in this case?

As with the LMA surgical airway access is beneficial when the cause of airway obstruction is proximal to the intervention. Cricothyroidotomy—the fastest and most readily performed surgical airway procedure—is therefore of benefit in patients who cannot be intubated and have airway obstruction involving the pharynx or larynx. This procedure may be accomplished by surgical opening of the cricothyroid membrane and placing an endotracheal tube into the trachea. Operative cricothyrotomy can be performed more rapidly than conventional tracheostomy; however, it is more traumatic to the larynx, and the cricothyrotomy tube should be removed after 24 hours. If the patient cannot be decannulated at this time, a conventional tracheostomy should replace the cricothyrotomy.

Tracheostomy, performed lower in the airway, requires more extensive surgical dissection, takes longer, and carries a greater risk of hemorrhage secondary to thyroid tissue trauma. Surgical access to the lower trachea might be necessary in the present case if the impaling object has transected or significantly disrupted the airway. This would be accomplished essentially through the wound itself but would require a partial or complete median sternotomy and the full resources of the OR.

Britt LD, Weireter LJ, Cole FJ. Management of acute neck injuries. In: Feliciano DV, Mattox KL, Moore EE, eds. *Trauma*. 6th ed. New York: McGraw-Hill; 2008:467–478.

C.14. What maintenance anesthetics are indicated or contraindicated in this patient?

If initial awake fiberoptic examination of the trachea (at the time of intubation) rules out an airway injury, then muscle relaxation to facilitate surgical exploration would be appropriate for the duration of the case. Any of the commonly used intermediate-acting nondepolarizing relaxants could be used. If an airway injury is present, then management of the patient using inhalational anesthesia alone, with continued spontaneous ventilation, offers additional security in the event of airway discontinuity during the course of surgical repair. Sevoflurane, because of its greater palatability, is the easiest volatile anesthetic to administer without interrupting the patient's ventilation. Care must be taken to ensure adequate fluid volume replacement during a pure inhalational anesthetic as hemodynamic instability is possible. Nitrous oxide is contraindicated when the potential for pneumothorax exists or when airway continuity is in doubt.

Narcotics certainly will be required for postoperative analgesia and may offer some intraoperative advantages as well. Once airway patency is assured, a narcotic-based anesthetic provides for the lowest level of circulating catecholamines, making it

easier to assess and manage fluid resuscitation. The usual concern with delayed emergence in a patient receiving a large dose of narcotics is not relevant in this case, as the patient will most likely require postoperative mechanical ventilation. The only caveat to intraoperative narcotics is the potential need to sustain spontaneous ventilation while the airway is assessed; narcotic administration should, therefore, be delayed until the anesthetic and surgical plans have become clear.

C.15. What complications will the surgical plan introduce?

Maintenance of homeostasis in the face of surgical provocations is the theme of many anesthetics and the present case is no exception. At some point—ideally after anesthetic induction, successful airway management, and placement of lines and monitors—the impaling object is going to be removed from the patient's neck. Blunt object impalements in patients seen alive in the trauma center may produce less organ-specific damage than predicted from the location and course of the injury due to the ability of mobile anatomic structures to deform away from low-speed penetrations. Even so, it is entirely possible that this object has injured one of the great vessels or the trachea and that removing it might lead to torrential bleeding or significant disruption of the airway. The anesthesia team must be prepared to change course rapidly from a spontaneous breathing inhalational approach (assuming that airway continuity is the initial concern) to a hemodynamically friendly narcotic-based approach if blood loss and hemorrhagic shock become the major issue. An open team discussion of both surgical and anesthetic plans, including likely contingencies, is highly recommended before beginning definitive treatment.

Dutton RP. Pathophysiology and treatment of traumatic shock. In Smith C, ed. *Trauma Anesthesia: Basic and Clinical Aspects*. Cambridge: Cambridge University Press; 2008:55–68.

D. Postoperative Management

D.1. What are the criteria for extubation?

Assuming that the case goes well and the patient's anatomic injuries are successfully repaired, it is appropriate to consider emergence and extubation when the following criteria are satisfied:

- Hemodynamic stability with complete cessation of bleeding and normal systemic coagulation.
- Adequate respiratory drive and reserve including complete return of neuromuscular function and minimal requirement for ventilator support.
- Acceptable mental status. The patient should be calm, cooperative, comfortable, not overly sedated, and recovered from acute intoxication. The patient should be able to follow commands.
- Evidence of airway patency. Edema at the site of injury will not be an issue with an endotracheal tube in place but might obstruct the airway quickly following extubation. Although not 100% predictive, the presence of an air leak around the endotracheal tube when the cuff is deflated is very reassuring.
- Completion of the diagnostic workup for "high-energy" trauma, including indicated CT scans and laboratory studies, and completion of all procedures are likely to require general anesthesia. It would be poor judgment to extubate the patient after tracheal repair only to have the orthopedic surgeons schedule him for urgent pelvic surgery.

Dutton RP, McCunn M, Grissom TE. Anesthesia for trauma. In Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier Churchill Livingstone; 2010:2277–2311.

D.2. What techniques may be used during extubation?

The best results from extubation will be achieved when the patient is most calm and comfortable and when the extubation itself is as nonstimulating as possible. The appropriate level of sedation and analgesia is a complicated, controversial, and very important question. Sedative agents such as benzodiazepines and propofol will diminish the patient's respiratory drive, cooperation, and ability to protect the airway, and should be minimized. The right level of narcotics, on the other hand, will allow for a comfortable patient with diminished airway reactivity, who can open their eyes and follow commands but is not otherwise distressed by the endotracheal tube or ventilator. The endotracheal tube should be suctioned ahead of time, and extubation deferred if there are copious secretions. Enough time should be allowed after suctioning for the stimulation to pass and the patient to relax. The posterior pharynx is then suctioned, the patient is asked to inhale deeply, the cuff is deflated, and the endotracheal tube is removed in one swift motion as the patient exhales.

The airway is in jeopardy immediately after extubation because edema and secretions may compromise respiratory function. Continuous pulse oximetry in a monitored setting is required and humidified oxygen should be administered for 24 hours postextubation.

D.3. How does alcohol abuse affect postoperative management?

Symptomatic withdrawal from alcohol usually occurs within 24 hours and manifests as agitation, tachycardia, and hypertension. Delirium tremens can occur thereafter if prophylactic therapy is not initiated. Prophylaxis should consist of a small basal dose of benzodiazepines or a low-dose intravenous alcohol infusion, with frequent assessment of mental status and the willingness to provide supplemental short-acting benzodiazepines if symptoms develop. The plan for delirium tremen prophylaxis should be coordinated with the pain management plan, ideally under the direction of a single individual, to provide for overall consistency and to avoid oversedation and respiratory arrest secondary to polypharmaceutical administration.

D.4. What pain medication should be used?

Postoperative analgesia in this case will depend on the extent of the surgical procedure and on the individual tolerance of the patient. Soft-tissue exploration of the neck, including surgery on the trachea or major vessels, requires relatively little postoperative analgesia. Titrated intravenous narcotics can be used in the first 24 hours with a rapid transition to an oral narcotic/acetaminophen preparation thereafter. Median sternotomy or other significant extension of the surgery into the chest will necessitate more intensive postoperative analgesia, including continuous narcotic infusion while the patient remains intubated, followed by intravenous patient-controlled analgesia after emergence and extubation. Nonsteroidal anti-inflammatory drugs are an appropriate adjuvant therapy once the risk of traumatic hemorrhage is past.

CHAPTER 34

Open-Eye Injury

THERESA T. KUDLAK

A 28-YEAR-OLD, OTHERWISE, HEALTHY MAN presented to the emergency room with a fishhook embedded in his eye. He had eaten a full meal just before the fishing accident.

A. Medical Disease and Differential Diagnosis

1. Why is this patient a particular challenge to the anesthesiologist?
2. What are the determinants of intraocular pressure (IOP) under normal circumstances? What is the normal range? What was the expected IOP in this patient's injured eye?
3. How is aqueous humor formed and eliminated?
4. How is IOP affected by arterial Pco_2, systemic blood pressure, coughing and vomiting, deep inspiration, and hypoxemia?
5. What is the role of the central nervous system (CNS) on IOP?
6. What is glaucoma?
7. Is atropine contraindicated in patients with glaucoma?
8. How do carbonic anhydrase inhibitors work to decrease IOP? By what mechanism may osmotic agents decrease IOP?
9. Are carbonic anhydrase inhibitors or osmotic diuretics indicated in open-globe injuries?
10. Are topically applied ophthalmic medications absorbed systemically? How can this absorption be reduced? Which eyedrops may have effects that are of concern to the anesthesiologist?

B. Preoperative Evaluation and Preparation

1. Is an open-globe injury always a surgical emergency?
2. What preoperative evaluation would you require?
3. The patient had eaten shortly before the accident. Would you attempt to pass a nasogastric tube or to administer emetics to empty the stomach?
4. Could this case be done with topical anesthesia or a retrobulbar block?
5. How would you premedicate this patient?

C. Intraoperative Management

1. What are some factors that may increase the risk of vitreous herniation during induction and maintenance of anesthesia?
2. Will you intubate this patient? Would you consider a laryngeal mask airway? How does intubation affect IOP? How can this effect be minimized?
3. Would you consider an awake intubation?
4. Is succinylcholine contraindicated in open-globe injuries? How does succinylcholine affect IOP?
5. Does pretreatment with nondepolarizing muscle relaxants prevent the succinylcholine-induced elevation in IOP?
6. How do nondepolarizing muscle relaxants affect IOP?
7. How will you perform a rapid-sequence induction and intubation without using succinylcholine?
8. What are the effects of ketamine on the eye?
9. Would you consider the use of etomidate as an induction agent? What about propofol?
10. How do inhalation agents affect IOP and by what mechanism?
11. During the procedure, the patient's pulse rate suddenly dropped to 40 beats per minute. What do you think was happening? What is the oculocardiac reflex (OCR)?
12. What are the afferent and efferent pathways of the OCR?
13. What factors contribute to the incidence of the OCR?
14. How do you diagnose and treat the OCR?
15. Is atropine useful for the OCR?
16. Can retrobulbar block prevent the OCR? Is it appropriate in this patient?

D. Postoperative Management

1. Would you reverse the neuromuscular blockade in this patient?
2. Do reversal doses of atropine affect IOP?
3. What would you do before extubating this patient?
4. When would you extubate this patient?
5. The patient awakened in the recovery room and complained of pain and tearing in the opposite eye. The conjunctiva was inflamed. What was the likely cause?
6. Will taping the eyes shut or applying ointment prevent corneal abrasions? Are there any contributing factors?
7. What should you do when you suspect that your patient might have a corneal abrasion?
8. A month after the surgical repair, the patient complained of impaired vision in the operative eye. He was examined and found to have a detached retina. As part of the surgical treatment, the ophthalmologist injected a gas bubble into the patient's posterior chamber. Why is this important to an anesthesiologist?

A. Medical Disease and Differential Diagnosis

A.1. Why is this patient a particular challenge to the anesthesiologist?

The combination of a full stomach and an open-globe injury presents a unique challenge to the anesthesiologist. In addition to the increased risk of aspiration of gastric contents, any drug or maneuver that raises IOP in the injured, open eye may cause extrusion of the vitreous humor and loss of vision when the globe is opened.

Cunningham AJ, Barry P. Intraocular pressure: physiology and implications for anesthetic management. *Can Anaesth Soc J.* 1986;33:195–208.

Holloway KB. Control of the eye during general anaesthesia for intraocular surgery. *Br J Anaesth.* 1980;52:671–679.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:2385.

A.2. What are the determinants of intraocular pressure (IOP) under normal circumstances? What is the normal range? What was the expected IOP in this patient's injured eye?

IOP is determined by the balance between production and drainage of aqueous humor, by changes in choroidal blood volume, and by vitreous volume and extraocular muscle tone. Resistance to outflow of aqueous humor in the trabecular tissue is probably the factor that maintains IOP within physiologic range, but the mechanism of homeostasis is unknown.

Normal IOP is 12 to 16 torr in the upright posture and increases by 2 to 4 torr in the supine position. IOP has been observed to nearly double in steep head down position in the operating room.

When the globe is open, the IOP is lowered and may be as low as ambient pressure. The concern in this case is for the relative volume of choroid and vitreous humor within the eye. If this volume should increase while the eye is opened, the vitreous humor may be lost. Any deformation of the eye by external pressure in the globe may cause an increase in IOP.

Cunningham AJ, Barry P. Intraocular pressure: physiology and implications for anaesthetic management. *Can Anaesth Soc J*. 1986;33:195–208.

Jay JL. Functional organization of the human eye. *Br J Anaesth.* 1980;52:649–654.

Kohli R, Ramsingh H, Makkad B. The anesthetic management of ocular trauma. *Int Anesthesiol Clin.* 2007;45:83–98.

Kumar C, Dodds C, Fanning G, eds. *Ophthalmic Anaesthesia.* Lisse, The Netherlands: Swets and Zeitlinger BV; 2002:23–25.

LeMay M. Aspects of measurement in ophthalmology. *Br J Anaesth.* 1980;52:655–662.

Miller RD, ed. *Miller's Anesthesia.* 7th ed. Philadelphia: Churchill Livingstone; 2010:2379.

Smith GB. *Ophthalmic Anaesthesia.* Baltimore: University Park Press; 1983:1–13.

A.3. How is aqueous humor formed and eliminated?

Aqueous humor is a clear fluid that occupies the anterior and posterior chambers of the eye. Its total volume is 0.3 mL. Aqueous humor is produced primarily by an active secretory process from the ciliary body in the posterior chambers at an equilibrium rate of 2 μL per minute. The aqueous then circulates through the pupil to the anterior chamber, passes through the trabeculated Fontana spaces, and enters Schlemm canal. From here, the fluid drains into the episcleral veins and finally into the cavernous sinus or jugular venous systems (Fig. 34.1).

Cunningham AJ, Barry P. Intraocular pressure: physiology and implications for anaesthetic management. *Can Anaesth Soc J*. 1986;33:195–208.

Jay JL. Functional organization of the human eye. *Br J Anaesth.* 1980;52:649–654.

LeMay M. Aspects of measurement in ophthalmology. *Br J Anaesth.* 1980;52:655–662.

McGoldrick K, ed. *Anesthesia for Ophthalmic and Otolaryngologic Surgery.* Philadelphia: WB Saunders; 1992:180–182.

Miller RD, ed. *Miller's Anesthesia.* 7th ed. Philadelphia: Churchill Livingstone; 2010:2379.

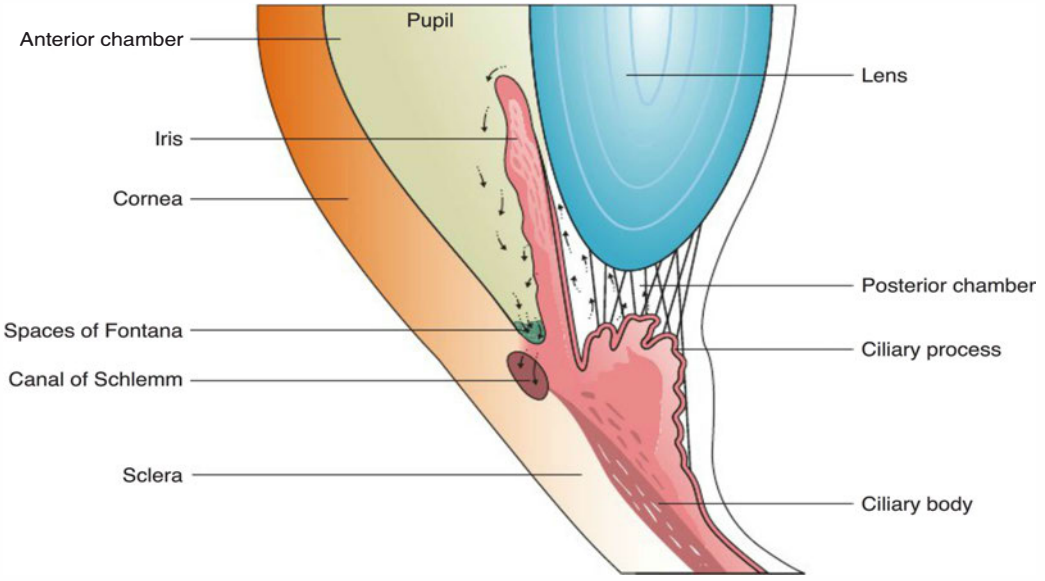

Figure 34.1 Sites of formation, circulation, and drainage of aqueous humor. (From Cunningham AJ, Barry B. Intraocular pressure: physiology and implications for anesthetic management. *Can Anaesth Soc J.* 1986;33:197, with permission.)

A.4. How is IOP affected by arterial Pco_2, systemic blood pressure, coughing and vomiting, deep inspiration, and hypoxemia?

The choroidal arterioles vasodilate in response to hypercapnia and constrict during hypocapnia, thereby changing intraocular volume and pressure. However, the effect is minimal within the normal physiologic range of Pco_2.

Minor fluctuations in arterial blood pressure also have minimal effects on IOP, although IOP may be seen to increase when hypertension is sustained and can fall significantly with induced hypotension. Changes in venous pressure, on the other hand, have a major impact on IOP. Vomiting, coughing, and bucking on the endotracheal tube cause a dramatic increase in IOP by 30 to 40 torr. These actions, and also Valsalva maneuver, cause congestion in the venous system, which impedes outflow of aqueous humor and increases the volume of choroidal blood. A deep inspiration may reduce IOP by 5 torr. Hypoxemia may increase IOP through choroidal vasodilatation.

Beulen P, Rotteveel J, de Ha, et al. Ultrasonographic assessment of congestion of the choroid plexus in relation to the carbondioxide pressure. *Eur J Ultrasound*. 2000;11:25–29.

Calobrisi BL, Lebowitz P. Muscle relaxants and the open globe. *Int Anesthesiol Clin*. 1990;28:83–88.

Cunningham AJ, Barry P. Intraocular pressure: physiology and implications for anaesthetic management. *Can Anaesth Soc J*. 1986;33:195–208.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:2379.

Murphy DF. Anesthesia and intraocular pressure. *Anesth Analg*. 1985;64:520–530.

Smith RB, Aass AA, Nemoto EM. Intraocular and intracranial pressure during respiratory alkalosis and acidosis. *Br J Anaesth*. 1981;53:967–972.

A.5. What is the role of the central nervous system (CNS) on IOP?

The CNS influences IOP through alterations in extraocular muscle tone or, indirectly, by hormonal or hemodynamic changes.

Cunningham AJ, Barry P. Intraocular pressure: physiology and implications for anaesthetic management. *Can Anaesth Soc J*. 1986;33:195–208.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:2379.

A.6. What is glaucoma?

Glaucoma is a pathologic elevation of IOP caused by increased resistance to outflow of aqueous humor from the anterior chamber of the eye. It is classified as either open- or closed-angle glaucoma, depending on the anatomy and pathophysiology. Chronic elevation of IOP interferes with the intraocular blood supply and normal metabolism of the cornea. It can result in corneal opacities or decreased retinal blood flow.

The pathophysiology in glaucoma involves increased resistance to the flow of aqueous humor through Fontana spaces as a result of scarring of the trabecular network or thickening of the endothelial covering of these channels. In closed-angle glaucoma, the iris bulges forward blocking the access of aqueous humor to the trabecular network. This may occur with pupillary dilation or an acutely swollen lens.

Johnson DH, Brubaker RF. Glaucoma: an overview. *Mayo Clin Proc*. 1986;61:59–67.

LeMay M. Aspects of measurement in ophthalmology. *Br J Anaesth*. 1980;52:655–662.

A.7. Is atropine contraindicated in patients with glaucoma?

Topical atropine in the eye is generally contraindicated in patients with glaucoma, especially in those with narrow-angle glaucoma. Atropine, studied in a single dose of 0.01 mg per kg, administered intramuscularly (IM), or given orally as 0.6 mg in 2 doses 4 hours apart, caused no increase in IOP in either open- or closed-angle glaucoma because by calculation, only approximately 0.0001 mg reaches the eye, which is far less than topical dose. Intravenous atropine is associated with mydriasis and might be contraindicated in patients with glaucoma; however, preemptive topical use of pupillary constrictors such as pilocarpine and timolol avoid this problem.

Adams AK, Jones RM. Anaesthesia for eye surgery: general considerations. *Br J Anaesth*. 1980;52:663–669.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1324–1325.

Greenstein SH, Abramson DH, Pitts R. Systemic atropine and glaucoma. *Bull N Y Acad Med*. 1984;60:961–968.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010: 2378–2386.

Rosen DA. Anesthesia in ophthalmology. *Can Anaesth Soc J*. 1962;9:545–549.

Schwartz, B. Current concepts in ophthalmology: the glaucomas. *N Engl J Med*. 1978; 299:182–184.

Schwartz H, deRoeth A Jr, Papper EM. Preanesthetic use of atropine in patients with glaucoma. *JAMA*. 1957;165:144.

A.8. How do carbonic anhydrase inhibitors work to decrease IOP? By what mechanism may osmotic agents decrease IOP?

Carbonic anhydrase inhibitors, such as acetazolamide, interfere with the sodium-pump mechanism necessary for secretion of aqueous humor. An intravenous dose acts in 5 minutes, with maximal effect in 20 to 30 minutes. Chronic acetazolamide therapy may result in potassium depletion.

Osmotic agents, such as mannitol, increase plasma oncotic pressure relative to that of aqueous humor and produce an acute, transient drop in IOP. The maximum reduction in IOP occurs after 30 to 45 minutes and the effect lasts 5 to 6 hours.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1325–1327.

McGoldrick KE. Ocular drugs and anesthesia. *Int Anesthesiol Clin*. 1990;28(2):72–77.

A.9. Are carbonic anhydrase inhibitors or osmotic diuretics indicated in open-globe injuries?

No. If the globe is open, the IOP is low and these agents are not useful. In addition, they may cause transient choroidal congestion, which could lead to loss of ocular contents.

Smith GB. *Ophthalmic Anaesthesia*. Baltimore: University Park Press; 1983.

A.10. Are topically applied ophthalmic medications absorbed systemically? How can this absorption be reduced? Which eyedrops may have effects that are of concern to the anesthesiologist?

Topical ophthalmic drugs may be absorbed through the conjunctiva or may drain through the nasolacrimal duct and be absorbed through the nasal mucosa. Absorption is increased when the eye is instrumented, diseased, or traumatized. Finger pressure on the inner canthus for a few minutes after instillation of eyedrops will impede absorption by occluding the nasolacrimal duct.

Usage of the following topical medications may have implications for the anesthesiologist:

Atropine

Atropine is used to produce mydriasis and cycloplegia. The 1% solution contains 0.2 mg to 0.5 mg of atropine per drop. Systemic reactions, seen primarily in children and older adults, include tachycardia, flushing, thirst, dry skin, and agitation. Atropine is contraindicated in closed-angle glaucoma.

Scopolamine

One drop of the 0.5% solution has 0.2 mg of scopolamine. CNS excitement can be treated with physostigmine, 0.015 mg per kg intravenously (IV), repeated one or two times in a 15-minute period. Scopolamine is contraindicated in closed-angle glaucoma.

Cyclopentolate (Cyclogyl)

Cyclopentolate, a short-acting mydriatic and cycloplegic, may cause transient neurotoxic effects such as incoherence, visual hallucinations, slurred speech, ataxia, and seizures. It is contraindicated in closed-angle glaucoma.

Tropicamide (Mydriacyl)

Tropicamide is used to produce mydriasis for refraction or funduscopic examination. It may have central nervous system (CNS) effects and can elevate IOP in closed-angle glaucoma.

Phenylephrine hydrochloride (Neo-Synephrine)

Phenylephrine hydrochloride is used to produce capillary decongestion and pupillary dilatation. Applied to the cornea, phenylephrine hydrochloride can cause palpitations, nervousness, tachycardia, headache, nausea and vomiting, severe hypertension, reflex bradycardia, and subarachnoid hemorrhage. Solutions of 2.5%, 5%, and 10% (6.25-mg phenylephrine per drop) are available. The dose is 1 drop per eye per hour of the 2.5% solution (children) or the 5% solution (adults).

Epinephrine

Topical 2% epinephrine will decrease aqueous secretion, improve outflow, and lower IOP in open-angle glaucoma. Side effects include hypertension, palpitations, fainting, pallor, and tachycardia. The effects last approximately 15 minutes. One drop of 2% solution contains 0.5 to 1 mg of epinephrine. Epinephrine 1:200,000 in a balanced salt solution is sometimes continuously infused into the anterior chamber during cataract surgery. Systemic effects may occur.

Timolol maleate (Timoptic)

Timolol maleate is a β-blocker used in the treatment of chronic glaucoma. Side effects include light-headedness, fatigue, disorientation, depressed CNS function, and exacerbation of asthma. Bradycardia and bronchospasm may occur as well as potentiation of systemic β-blockers.

Betaxolol HCl (Betoptic)

Betaxolol HCl is a cardioselective (β-1) blocking agent used to treat glaucoma. It may be hazardous in patients with sinus bradycardia, heart block, or heart failure.

Acetylcholine

Acetylcholine may be injected intraoperatively into the anterior chamber to produce miosis. Side effects are due to its parasympathetic action and include hypotension, bradycardia, and bronchospasm. Intravenous atropine is an effective treatment.

Echothiophate iodide (Phospholine iodide)

Echothiophate iodide, a cholinesterase inhibitor, is used as a miotic agent. It may prolong the effect of both succinylcholine and ester-type local anesthetics. Levels of pseudocholinesterase decrease by 80% after 2 weeks on the drug. It takes 3 to 6 weeks for return to normal pseudocholinesterase activity after stopping the drug (4 weeks for return to 75% activity). Succinylcholine and ester-type local anesthetics should be avoided. Demecarium is another such cholinesterase inhibitor.

Cocaine

Cocaine is used to produce vasoconstriction and to shrink mucous membranes during dacryocystorhinostomy. One drop of 4% solution contains approximately 1.5 mg of cocaine, and the maximum dose is approximately 3 mg per kg. Systemic effects may be seen with a dose as low as 20 mg and involve the CNS, respiratory, and cardiovascular systems.

Ballin N, Becker B, Goldman ML. Systemic effects of epinephrine applied topically to the eye. *Invest Ophthalmol.* 1966;5:125.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1327–1329.

Fraunfelder FW, Fraunfelder FT, Jensvold B. Adverse systemic effects from pledgets of topical ocular phenylephrine 10%. *Am J Ophthalmol*. 2002;134:624–625.

Johnson DH, Brubaker RF. Glaucoma: an overview. *Mayo Clin Proc*. 1986;61:59–67.

Lansche RK. Systemic reactions to topical epinephrine and phenylephrine. *Am J Ophthalmol*. 1966;61:95–98.

McGoldrick KE. Ocular drugs and anesthesia. *Int Anesthesiol Clin*. 1990;28(2):72–77.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:2379–2381.

deRoetth A Jr, Dettbarn WD, Rosenberg P, et al. Effect of phospholine iodine on blood cholinesterase levels of normal and glaucoma subjects. *Am J Ophthalmol*. 1965;59:586–592.

B. Preoperative Evaluation and Preparation

B.1. Is an open-globe injury always a surgical emergency?

No. In most cases, surgery is not required immediately and some time may be spent in adequately preparing the patient for anesthesia and surgery. However, the surgery should probably be performed within 12 hours to minimize the possibility of infection and other complications. Delaying surgery for gastric emptying to occur is not reliable as gastric emptying may be prolonged in this stressful situation.

Arthur DS, Dewar KMS. Anaesthesia for eye surgery in children. *Br J Anaesth*. 1980;52:681–686.

Kohli R, Ramsingh H, Makkad B. The anesthetic management of ocular trauma. *Int Anesthesiol Clin*. 2007;45:83–98.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:2385.

Smith GB. *Ophthalmic Anaesthesia*. Baltimore: University Park Press; 1983:44–49.

B.2. What preoperative evaluation would you require?

An accurate, thorough history, and physical examination are the best means of evaluating this patient preoperatively and should reveal any existing medical problems that will guide your selection of preoperative laboratory tests.

In this otherwise healthy young patient, no routine laboratory tests are indicated, unless they are required by the institution in which you are practicing. In cases in which more extensive trauma is suspected, other injuries also must be addressed such as fractures to the skull and orbit, intracranial hemorrhage, and other injuries as suggested by the history and physical examination.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1336–1337.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:2385.

B.3. The patient had eaten shortly before the accident. Would you attempt to pass a nasogastric tube or to administer emetics to empty the stomach?

Absolutely not. These procedures are contraindicated when there has been a perforation of the eye. Gagging, vomiting, and straining could cause a potentially

disastrous increase in IOP and extrusion of intraocular contents. A cough can increase central venous pressure and choroidal blood volume and may raise IOP by 34 to 40 torr.

Adams AK, Jones RM. Anaesthesia for eye surgery: general considerations. *Br J Anaesth.* 1980;52:663–669.

Arthur DS, Dewar KM. Anaesthesia for eye surgery in children. *Br J Anaesth.* 1980;52: 681–688.

Cunningham AJ, Barry P. Intraocular pressure: physiology and implications for anaesthetic management. *Can Anaesth Soc J.* 1986;33:195–208.

Kohli R, Ramsingh H, Makkad B. The anesthetic management of ocular trauma. *Int Anesthesiol Clin.* 2007;45:83–98.

B.4. Could this case be done with topical anesthesia or a retrobulbar block?

General anesthesia is the preferred technique for open-globe injuries: the patient is fully immobile and there is no time limit for the procedure. In this case where the patient is not fasting, an endotracheal tube will guard against aspiration.

A retrobulbar or peribulbar injection has the potential to increase IOP because of the volume of local anesthetic used and the likelihood of the patient squeezing his eyes during the injection. However, there have been reports of successful use of blocks for repair of open-globe injuries. Topical anesthesia with intravenous (IV) sedation also has been used to repair the globe in select patients with limited injury when general anesthesia is contraindicated.

Boscia F, La Tegola MG, Columbo G, et al. Combined topical anesthesia and sedation for open-globe injuries in selected patients. *Ophthalmology.* 2003;110:1555–1559.

Lo MW, Chalfin S. Retrobulbar anesthesia for repair of ruptured globes. *Am J Ophthalmol.* 1997;123:833–835.

Scott IU, McCabe CM, Flynn HW, et al. Local anesthesia with intravenous sedation for surgical repair of selected open globe injuries. *Am J Ophthalmol.* 2002;134:707–711.

B.5. How would you premedicate this patient?

Premedications should be given parenterally because gastrointestinal absorption is unreliable. Sedatives and anxiolytics may be given as necessary. Metoclopramide (0.15 mg per kg IM or IV) may be used to facilitate gastric emptying and to increase the tone of the cardiac sphincter. Narcotics should be used cautiously because they may cause nausea and vomiting. Nonparticulate antacids and H_2 receptor antagonists (cimetidine 2 mg per kg IM) should be considered to reduce the risk of aspiration pneumonitis. Intravenous droperidol (0.01 mg per kg) or ondansetron (0.1 mg per kg) can be given for antiemesis.

Atropine or glycopyrrolate will be useful to reduce secretions and gastric acidity and they may also inhibit the OCR.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia.* 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1336.

Cunningham AJ, Barry P. Intraocular pressure: physiology and implications for anaesthetic management. *Can Anaesth Soc J.* 1986;33:195–208.

Smith GB. *Ophthalmic Anaesthesia.* Baltimore: University Park Press; 1983:44–49.

C. Intraoperative Management

C.1. What are some factors that may increase the risk of vitreous herniation during induction and maintenance of anesthesia?

Factors that may increase the risk of vitreous herniation during induction and maintenance of anesthesia include the following:

- Face mask pressing on the eyeball
- Increased pressure from coughing, straining, bucking, and head-down position
- Extraocular muscle spasm induced by depolarizing muscle relaxants or surgical stimulation during light anesthesia
- Poorly applied cricoid pressure that blocks venous drainage from the eye
- Choroidal congestion from hypercarbia, hypoxia, osmotic diuretics, intubation, or increases in blood pressure

Cunningham AJ, Barry P. Intraocular pressure: physiology and implications for anaesthetic management. *Can Anaesth Soc J*. 1986;33:195–208.

Holloway KB. Control of the eye during general anaesthesia for intraocular surgery. *Br J Anaesth*. 1980;52:671–679.

Kohli R, Ramsingh H, Makkad B. The anesthetic management of ocular trauma. *Int Anes Clinics* 2007;45:83–98.

Libonati MM, Leahy JJ, Ellison N. The use of succinylcholine in open-eye surgery. *Anesthesiology*. 1985;62:637–640.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:2378–2385.

C.2. Will you intubate this patient? Would you consider a laryngeal mask airway? How does intubation affect IOP? How can this effect be minimized?

It is imperative that this patient be intubated not only to maintain the airway, which is close to the surgical field, but also to avoid pressure by a face mask on the eyeball and to minimize the risk of aspiration. Although the laryngeal mask airway has been used successfully in ophthalmologic anesthesia, it is not appropriate in this case because it does not protect the airway from aspiration. Many studies have demonstrated a significant increase in IOP caused by laryngoscopy and intubation under varying states of anesthetic depth and muscle relaxation. IOP may be increased even when there is no visible reaction to intubation. This increase in IOP can be attenuated by topical laryngeal anesthesia and by increased depth of anesthesia to reduce coughing, straining, and increases in blood pressure. The cardiovascular response to intubation can also be reduced by intravenous lidocaine (1.5 mg per kg), β-blockers, α-2 agonists, or calcium channel blockers. Topical anesthesia of the larynx is not recommended in a full-stomach situation because of the increased risk of aspiration.

Akhtar TM, McMurray P, Kerr WJ, et al. A comparison of laryngeal mask airway with tracheal tube for intra-ocular ophthalmic surgery. *Anaesthesia*. 1992;47:668–671.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1336–1337.

Cook JH. The effect of suxamethonium on intraocular pressure. *Anaesthesia*. 1981;36:359–365.

Gefke K, Andersen LW, Friesel H. Lidocaine given intravenously as a suppressant of cough and laryngospasm with extubation after tonsillectomy. *Acta Anaesthesiol Scand*. 1983;27:111–112.

Libonati MM, Leahy JJ, Ellison N. The use of succinylcholine in open eye surgery. *Anesthesiology*. 1985;62:637–640.

Miller RD, ed. *Miller's Anesthesia.* 7th ed. Philadelphia: Churchill Livingstone; 2010:2385.

Smith RB, Aass AA, Nernoto EM. Intraocular and intracranial pressure during respiratory alkalosis and acidosis. *Br J Anaesth.* 1981;53:967–972.

C.3. Would you consider an awake intubation?

Awake intubation is frequently accompanied by coughing and bucking and is risky in an open-globe injury when other safe methods of intubation are available. However, when dealing with a possible compromised airway or difficult intubation, an awake fiber-optic intubation expertly done under careful sedation may be indicated to safely secure the airway.

Calobrisi BL, Lebowitz P. Muscle relaxants and the open globe. *Int Anesthesiol Clin.* 1990;28(2):83–88.

Kohli R, Ramsingh H, Makkad B. The anesthetic management of ocular trauma. *Int Anesthesiol Clin.* 2007;45:83–98.

Miller RD, ed. *Miller's Anesthesia.* 7th ed. Philadelphia: Churchill Livingstone; 2010:2378–2385.

C.4. Is succinylcholine contraindicated in open-globe injuries? How does succinylcholine affect IOP?

The use of succinylcholine in open-globe injuries is controversial. In the intact eye, following thiopental induction, succinylcholine has been shown to increase IOP by 6 to 8 torr between 1 and 4 minutes after administration. Tracheal intubation further increases IOP. IOP returns to baseline in 5 to 7 minutes. In open-globe injuries, succinylcholine use has been associated with loss of ocular contents. The increase in IOP may be mediated by prolonged tonic contraction of the extraocular muscles, although IOP has been shown to rise after succinylcholine even when the extraocular muscles have been severed. Other factors that may be contributory include choroidal blood flow, increased central venous pressure, and increased resistance to outflow of aqueous humor resulting from the cycloplegic effects of succinylcholine.

The hemodynamic response to laryngoscopy or intubation may have a much more significant effect on IOP than succinylcholine alone. Simply blinking will raise the IOP in a normal eye by 10 to 15 torr, similar to the effect of succinylcholine. Pretreating with nifedipine or lidocaine, which deepens the anesthesia, may attenuate the increase in IOP following succinylcholine and intubation.

Calobrisi BL, Lebowitz P. Muscle relaxants and the open globe. *Int Anesthesiol Clin.* 1990;38(2):83–88.

Cook JH. The effect of suxamethonium on intraocular pressure. *Anaesthesia.* 1981;36: 359–365.

Cunningham AJ, Barry P. Intraocular pressure: physiology and implications for anaesthetic management. *Can Anaesth Soc J.* 1986;33:195–208.

Holloway KG. Control of the eye during general anaesthesia for intraocular surgery. *Br J Anaesth.* 1980;52:671–679.

Kelly RE, Dinner M, Turner LS, et al. Succinylcholine increases intraocular pressure in the human eye with the extraocular muscles detached. *Anesthesiology.* 1993;79:948–952.

Kohli R, Ramsingh H, Makkad B. The anesthetic management of ocular trauma. *Int Anes Clinics.* 2007;45:83–98.

Lincoff HA, Ellis CH, Devoe AG, et al. The effect of succinylcholine on intraocular pressure. *Am J Ophthalmol.* 1955;40:501–510.

Miller RD, ed. *Miller's Anesthesia.* 7th ed. Philadelphia: Churchill Livingstone; 2010: 2378–2385.

Moreno RJ, Kloess P, Carlson DW. Effect of succinylcholine on the intraocular contents of open globes. *Ophthalmology*. 1991;98:636–638.

Murphy DS, Davis MJ. Succinylcholine use in emergency eye operation. *Can J Anaesth*. 1987;34:101–102.

Smith RB, Babinski M, Leano N. The effect of lidocaine on succinylcholine-induced rise in intraocular pressure. *Can Anaesth Soc J*. 1979;26:482–483.

C.5. Does pretreatment with nondepolarizing muscle relaxants prevent the succinylcholine-induced elevation in IOP?

Available data are contradictory on this question, probably reflecting different methods of IOP measurement under varying depths of anesthesia with a variety of anesthetic adjuvant agents. Many techniques have been tried to prevent succinylcholine-induced elevation of IOP, and none has been consistently effective. However, there is no published report of loss of ocular contents when succinylcholine use has been preceded by pretreatment with a nondepolarizing relaxant and barbiturate for induction, and many anesthesiologists feel this is a safe combination for rapid-sequence induction in the open-eye, full-stomach situation.

Bourke DL. Open-eye injuries. *Anesthesiology*. 1985;63:727.

Calobrisi BL, Lebowitz P. Muscle relaxants and the open globe. *Int Anesthesiol Clin*. 1990;28(2):83–88.

Cunningham AJ, Barry P. Intraocular pressure: physiology and implications for anaesthetic management. *Can Anaesth Soc J*. 1986;33:195–208.

Hartman GS, Fiamengo SA, Riker WF Jr. Succinylcholine: mechanism of fasciculations and their prevention by d-tubocurarine or diphenylhydantoin. *Anesthesiology*. 1986;65:405–413.

Holloway KB. Control of the eye during general anaesthesia for intraocular surgery. *Br J Anaesth*. 1980;52:671–679.

Konchigeri HN, Lee YE, Venugopal K. Effect of pancuronium on intraocular pressure changes induced by succinylcholine. *Can Anaesth Soc J*. 1979;26:479.

Libonati MM, Leahy JJ, Ellison N. The use of succinylcholine in open-eye surgery. *Anesthesiology*. 1985;62:637–640.

McGoldrick KE. The open globe: is an alternative to succinylcholine necessary? *J Clin Anesth*. 1993;5:1–4.

Meyers EF, Krupin T, Johnson M, et al. Failure of nondepolarizing neuromuscular blockers to inhibit succinylcholine-induced increased intraocular pressure: a controlled study. *Anesthesiology*. 1978;48:149–151.

Miller RD, Way WL, Hickey RF. Inhibition of succinylcholine-induced increased intraocular pressure by nondepolarizing muscle relaxants. *Anesthesiology*. 1968;29:123–126.

Murphy DF. Anesthesia and intraocular pressure. *Anesth Analg*. 1985;64:520–530.

C.6. How do nondepolarizing muscle relaxants affect IOP?

Nondepolarizing muscle relaxants either decrease or have no effect on IOP.

Abbott MA, Samuel JR. The control of IOP during the induction of anaesthesia for emergency eye surgery. A high-dose vecuronium technique. *Anaesthesia*. 1987;42:1008–1012.

Agarwal LP, Mathur SP. Curare in ocular surgery: report of 25 cases. *Br J Ophthalmol*. 1952;36:603–610.

Calobrisi BL, Lebowitz P. Muscle relaxants and the open globe. *Int Anesthesiol Clin*. 1990;28(2):83–88.

Cunningham AJ, Kelly CP, Farmer J, et al. The effect of metocurine and metocurine-pancuronium combination in intraocular pressure. *Can Anaesth Soc J*. 1982;29:617–621.

Litwiller RW, DiFazio CA, Rushia EL. Pancuronium and intraocular pressure. *Anesthesiology*. 1975;42:750–752.

Maharaj RJ, Humphrey D, Kaplan N, et al. Effects of atracurium on intraocular pressure. *Br J Anaesth*. 1984;56:459–463.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:2378–2386.

Schneider MJ, Stirt JA, Finholt DA. Atracurium, vecuronium, and intraocular pressure in humans. *Anesth Analg*. 1986;65:877–882.

C.7. How will you perform a rapid-sequence induction and intubation without using succinylcholine?

The safety of the patient always must be the primary concern; the preservation of the injured eye is secondary. Measures must be taken to guarantee adequate anesthetic depth and to blunt the hemodynamic responses to laryngoscopy and endotracheal intubation. Pretreatment measures such as narcotics, β-blockers, calcium channel blockers, lidocaine, or midazolam should be considered. Before induction, the patient should breathe 100% oxygen for several minutes, administered by a gently applied face mask. Anesthesia can then be induced using carefully applied cricoid pressure with intravenous sodium thiopental (5 mg per kg) or propofol (2 to 3 mg per kg) and a nondepolarizing muscle relaxant. Several options exist:

- Pancuronium (0.15 to 0.2 mg per kg) will provide intubation condition in 90 seconds. Tachycardia and prolonged muscle relaxation may be a problem.
- Atracurium (0.5 mg per kg) will allow safe intubation in 3 minutes. A larger bolus (1.5 mg per kg) will allow intubation in 60 to 90 seconds but may cause hypotension, tachycardia, and histamine release.
- Cisatracurium—because of its intermediate onset of action, cisatracurium (0.10 to 0.15 mg per kg) is not recommended for rapid-sequence endotracheal intubations. Cisatracurium (0.4 mg per kg) 8 $\times$ ED95 will allow intubation in 90 seconds without histamine release, but duration of action may exceed for 60 minutes.
- Vecuronium (0.2 mg per kg) should provide adequate intubating conditions after 90 seconds.
- Rocuronium (0.8 to 1.0 mg per kg) gives excellent intubating conditions at 60 to 70 seconds. Time to recovery is variable and may take 45 to 60 minutes.
- An alternative is to pretreat the patient with a small dose of the nondepolarizing relaxant several minutes before induction, which may shorten the onset of action and lessen the dose required of subsequently administered relaxant. This has been referred to as a priming dose. Its use is controversial in that it may lead to diplopia, muscle weakness, respiratory distress, and aspiration while offering no definite advantage over the use of larger initial doses of nondepolarizing muscle relaxants. The doses for rapid tracheal intubation with succinylcholine or various nondepolarizing relaxants are listed in Chapter 14, section C.4, Table 14.4.

Whatever technique is selected, it is essential to monitor the degree of muscle relaxation with a neuromuscular blockade monitor. It is also possible to intubate the patient without any muscle relaxant at all after a deep level of anesthesia has been reached, but this is not a recommended technique. Not only is the airway unprotected for a long period, but also prevention of bucking cannot be guaranteed and positive pressure ventilation by face mask may exert pressure on the eye.

Abbott MA. The control of intraocular pressure during the induction of anaesthesia for emergency eye surgery. A high-dose vecuronium technique. *Anaesthesia*. 1987;42:1008–1012.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1336–1337.

Brown EM, Krishnaprasad D, Smiler BG. Pancuronium for rapid induction technique for tracheal intubation. *Can Anaesth Soc J*. 1979;26:489–491.

Foldes F. Rapid tracheal intubation with non-depolarizing neuromuscular blocking drugs: the priming principle. *Br J Anaesth*. 1984;56:663.

Lennon RL, Olson RA, Gronert GA. Atracurium or vecuronium for rapid sequence endotracheal intubation. *Anesthesiology*. 1986;64:510–513.

Mehta MP, Choi WW, Geris SD, et al. Facilitation of rapid endotracheal intubations with divided doses of nondepolarizing neuromuscular blocking drugs. *Anesthesiology*. 1985;62:392–395.

Musich J, Walts LF. Pulmonary aspiration after a priming dose of vecuronium. *Anesthesiology*. 1986;64:517–519.

Rich AL, Witherspoon CD, Morris RE, et al. Use of nondepolarizing anesthetic agents in penetrating ocular injuries. *Anesthesiology*. 1986;65:108–109.

Schneider MJ, Stirt JA, Finholt DA. Atracurium, vecuronium, and intraocular pressure in humans. *Anesth Analg*. 1986;65:877–882.

Sosis MB. On use of priming with vecuronium in a patient with an open globe and a full stomach. *Anesth Analg*. 1990;70:336–337.

C.8. What are the effects of ketamine on the eye?

Ketamine may cause nystagmus and blepharospasm and is, therefore, not suitable for ophthalmic surgery. Studies with respect to the effect of ketamine on IOP have shown both increased and decreased IOP in children and no change in IOP in adults premedicated with diazepam and meperidine. This may depend on whether ketamine is administered through the IM or IV route.

Antal M. Ketamine anesthesia and intraocular pressure. *Ann Ophthalmol*. 1978;10:1281–1284, 1289.

Ausinsch B, Rayborn RL, Munson ES, et al. Ketamine and intraocular pressure in children. *Anesth Analg*. 1976;55:773–775.

Cunningham AJ, Barry P. Intraocular pressure: physiology and implication for anaesthetic management. *Can Anaesth Soc J*. 1986;33:195–208.

Peuler M, Glass DD, Arens JF. Ketamine and intraocular pressure. *Anesthesiology*. 1975;5:575–578.

Yoshikawa K, Murai Y. The effect of ketamine on intraocular pressure in children. *Anesth Analg*. 1971;50:199–202.

C.9. Would you consider the use of etomidate as an induction agent? What about propofol?

Although etomidate has been associated with a decrease in IOP when used as an induction agent, the unpredictable incidence of generalized myoclonus seen with etomidate use and resultant elevation of IOP may preclude its use in open-globe injuries, unless rapid and complete prior muscle relaxation can be guaranteed. Propofol, with its antiemetic properties and ability to decrease IOP, would be an excellent choice for induction.

Berry JM, Merin RG. Etomidate myoclonus and the open globe. *Anesth Analg*. 1989;69:256–259.

Calla S, Gupta A, Sen N, et al. Comparison of the effects of etomidate and thiopentone on intraocular pressure. *Br J Anaesth.* 1987;59:437–439.

Ferrari LR, Donlon JV. A comparison of propofol, midazolam, and methohexital for sedation during retrobulbar and peribulbar block. *J Clin Anesth.* 1992;4:93–96.

Kohli R, Ramsingh H, Makkad B. The anesthetic management of ocular trauma. *Int Anes Clinics*. 2007;45:83–98.

Miller RD, ed. *Miller's Anesthesia.* 7th ed. Philadelphia: Churchill Livingstone; 2010:2378–2385.

C.10. How do inhalation agents affect IOP and by what mechanism?

Inhalation agents cause dose-related decreases in IOP as a consequence of the following:

- Reduced aqueous humor production
- Depression of the CNS control center
- Facilitation of aqueous humor outflow
- Decreased extraocular muscle tension
- Lowered arterial blood pressure

The degree of IOP reduction is proportional to the depth of anesthesia.

Cunningham AJ, Barry P. Intraocular pressure: physiology and implications for anaesthetic management. *Can Anaesth Soc J*. 1986;33:195–208.

Miller RD, ed. *Miller's Anesthesia.* 7th ed. Philadelphia: Churchill Livingstone; 2010:2379.

C.11. During the procedure, the patient's pulse suddenly dropped to 40 beats per minute. What do you think was happening? What is the oculocardiac reflex (OCR)?

The OCR may be manifested by bradycardia, bigeminy, ectopy, nodal rhythms, atrioventricular block, and cardiac arrest. It is caused by traction on the extraocular muscles (especially medial rectus), ocular manipulation, or manual pressure on the globe. The OCR is commonly seen during eye muscle surgery, detached retina repair, or enucleation or whenever there is extensive traction or rotation of the eyeball.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia.* 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1327.

Miller RD, ed. *Miller's Anesthesia.* 7th ed. Philadelphia: Churchill Livingstone; 2010:2379.

C.12. What are the afferent and efferent pathways of the OCR?

The OCR is trigeminovagal. The afferent pathway is by way of the ciliary ganglion to the ophthalmic division of the trigeminal nerve and through the gasserian ganglion to the main sensory nucleus in the fourth ventricle. The efferent pathway is the vagus nerve.

Adams AK, Jones RM. Anaesthesia for eye surgery: general considerations. *Br J Anaesth.* 1980;52:663–669.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia.* 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1327.

Smith GB. *Ophthalmic Anesthesia.* Baltimore: University Park Press; 1983:66–72.

C.13. What factors contribute to the incidence of the OCR?

Preoperative anxiety, light general anesthesia, hypoxia, hypercarbia, and increased vagal tone because of age or drugs. The reported incidence of cardiac rhythm changes during eye muscle surgery is 32% to 82%. The incidence is higher in children.

Miller RD, ed. *Miller's Anesthesia.* 7th ed. Philadelphia: Churchill Livingstone; 2010:2379.

Smith GB. *Ophthalmic Anesthesia.* Baltimore: University Park Press; 1983:66–72.

C.14. How do you diagnose and treat the OCR?

- Monitor the electrocardiogram intraoperatively and during any eye manipulation.
- Stop the surgical stimulus immediately.
- Ensure that ventilation is adequate.
- Ensure sufficient anesthetic depth.

The OCR may fatigue with repeated stimulation.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:2379.

Smith GB. *Ophthalmic Anesthesia.* Baltimore: University Park Press; 1983:66–72.

C.15. Is atropine useful for the OCR?

Atropine use is controversial. Atropine, 0.4 mg IM, as a premedicant has no vagolytic effect after 60 minutes and is of no value in preventing or treating the OCR. Atropine, 0.4 mg IV, is effective for 30 minutes in preventing bradycardia associated with the OCR. Doses greater than 0.5 mg IV can cause tachycardia, which may be detrimental in certain patients with heart disease. At least 2 to 3 mg is required to ensure a total vagal block.

Blanc VF. Anticholinergic premedication for infants and children on the oculocardiac reflex [Letter]. *Can Anaesth Soc J*. 1983;30:683–684.

Miller RD, ed. *Miller's Anesthesia.* 7th ed. Philadelphia: Churchill Livingstone; 2010: 2378–2386.

Steward DJ. Anticholinergic premedication in infants and children on the oculocardiac reflex [Reply]. *Can Anaesth Soc J*. 1983;30:684.

C.16. Can retrobulbar block prevent the OCR? Is it appropriate in this patient?

Retrobulbar block injection is not only unreliable in preventing the OCR but may, during the injection, cause OCR, cardiac arrest, or retrobulbar hemorrhage.

Local infiltration of the recti muscles and a delicate operating technique may decrease the incidence of OCR. In this patient, retrobulbar block is relatively contraindicated because it may increase IOP.

Allen ED, Elkington AR. Local anesthesia and the eye. *Br J Anaesth.* 1980;52:689–694.

McGoldrick KE. Complications of regional anesthesia for ophthalmic surgery. *Yale J Biol Med*. 1993;66:443–445.

Miller RD, ed. *Miller's Anesthesia.* 7th ed. Philadelphia: Churchill Livingstone; 2010:2379.

D. Postoperative Management

D.1. Would you reverse the neuromuscular blockade in this patient?

There is no contraindication to reversal, provided that efforts are made to minimize coughing or bucking on the endotracheal tube.

D.2. Do reversal doses of atropine affect IOP?

Reversal doses of atropine, when given in conjunction with neostigmine, do not significantly alter IOP and this combination may be safely used, even in patients with glaucoma.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia.* 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009;1325.

Cunningham AJ, Barry P. Intraocular pressure: physiology and implications for anaesthetic management. *Can Anaesth Soc J.* 1986;33:195–208.

D.3. What would you do before extubating this patient?

- Empty the stomach with an orogastric tube while the patient is still paralyzed.
- Suction the pharynx with the patient still paralyzed or deeply anesthetized.
- Give an antiemetic, such as droperidol 0.01 mg per kg IV or ondansetron 0.1 mg per kg IV, 20 to 30 minutes before the end of surgery.
- Give lidocaine 1.5 mg per kg IV or remifentanil 0.5 to 0.8 μg per kg IV to prevent coughing during emergence.

Gefke K, Anderson LW, Friesel E. Intravenous lidocaine as a suppressant of cough and laryngospasm with extubation after tonsillectomy. *Acta Anaesthesiol Scand.* 1983;27:111–112.

Miller RD, ed. *Miller's Anesthesia.* 7th ed. Philadelphia: Churchill Livingstone; 2010:2385.

D.4. When would you extubate this patient?

There may be a conflict between the desire to extubate awake because of the full stomach and the desire to extubate deep to prevent coughing and bucking. Because modern techniques of eye repair involve minimal risk of suture disruption with coughing, one may extubate awake, thereby protecting the airway.

D.5. The patient awakened in the recovery room and complained of pain and tearing in the opposite eye. The conjunctiva was inflamed. What was the likely cause?

General anesthesia decreases tear production and reduces normal mechanical eyelid closure. Corneal abrasions are the most common perioperative ocular injury, and this patient's complaints are consistent with that diagnosis.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia.* 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1340.

Miller RD, ed. *Miller's Anesthesia.* 7th ed. Philadelphia: Churchill Livingstone; 2010:2385.

D.6. Will taping the eyes shut or applying ointment prevent corneal abrasions? Are there any contributing factors?

There is no guarantee that an eye that has been taped shut or lubricated will not sustain a corneal abrasion. Most anesthesiologists protect the eyes in some way; however, abrasions still occur. Corneal abrasions represent the most common ophthalmic complication associated with general anesthesia. The incidence may be as high as 44% when no preventative measures have been taken and the cornea is exposed. The mechanism is thought to be drying of or direct trauma to exposed cornea. Possible contributing factors may be mask anesthesia, prone position, or having the patient's face in the surgical field.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1340.

Bronheim D, Abel M, Neustein S. Corneal abrasions following non-ophthalmic surgery: a retrospective view of 35,253 general anesthetics. *Anesthesiology*. 1995;83:A1071.

Gild WM, Posner KL, Caplan RA, et al. Eye injuries associated with anesthesia. *Anesthesiology*. 1992;76:204–208.

D.7. What should you do when you suspect your patient might have a corneal abrasion?

Prompt consultation with an ophthalmologist should be solicited for precise diagnosis and treatment. The patient should be reassured that corneal abrasions usually heal and that relief of pain occurs within 24 to 48 hours. Possible treatments include eye patching and topical administration of antibiotics, short-acting cycloplegics, or anti-inflammatory agents. The use of eye patches is controversial.

A topical anesthetic for the cornea should never be given to a patient for self-administration. Misuse may cause delayed wound healing and keratopathy.

Hulbert MF. Efficacy of eye pad in corneal healing after corneal foreign body removal. *Lancet*. 1991;337:643.

Jampel HD. Patching for corneal abrasions. *JAMA*. 1995;274:1504.

Kaiser PK. The Corneal Abrasion Patching Study Group. A comparison of pressure patching versus no patching for corneal abrasions sue to trauma or foreign body removal. *Ophthalmology*. 1995;102:1936–1942.

D.8. A month after the surgical repair, the patient complained of impaired vision in the operative eye. He was examined and found to have a detached retina. As part of the surgical treatment, the ophthalmologist injected a gas bubble into the patient's posterior chamber. Why is this important to an anesthesiologist?

If a patient with intraocular gas needs to undergo general anesthesia before the gas bubble resorbs, nitrous oxide must be avoided because the gas will expand thereby increasing IOP. The effects on the eye may be disastrous. Various types of gasses may be injected, with different durations. Patients are usually given bracelets to inform anesthesiologists that they have gas in their eye and nitrous oxide must be avoided.

Fu AD, McDonald HR, Eliott D, et al. Complications of general anesthesia using nitrous oxide in eyes with preexisting gas bubbles. *Retina*. 2002;22(5):569–574.

Hart RH, Vote BJ, Borthwick JH, et al. Loss of vision caused by expansion of intraocular perfluoropropane (C_3 F_8) gas during nitrous oxide anesthesia. *Am J Ophthalmol*. 2002;134(5):761–763.

CHAPTER 35

Laser Treatment for Laryngeal Lesions

MARCUS GUTZLER

A 7-YEAR-OLD GIRL

with a past history of recurrent respiratory papillomatosis (RRP) is scheduled for direct laryngoscopy and possible reexcision. The patient has had 10 papilloma reexcisions over the course of the previous 2 years. Currently, she is undergoing adjuvant treatment with α-interferon, but now presents again with slowly progressive hoarseness.

A. Medical Disease and Differential Diagnosis

1. What is the cause of RRP?
2. Does delivery through cesarean section prevent infection of the neonate with human papilloma virus (HPV)?
3. Is this an unusual presentation for RRP?
4. What are the available treatment options for RRP?
5. What are common adverse effects of α-interferon therapy?
6. What is the differential diagnosis of hoarseness in this child?

B. Preoperative Evaluation and Preparation

1. What are the key points of the preanesthetic history and physical examination in this patient?
2. What preoperative laboratory tests are necessary?
3. How should this child be premedicated before coming to the operating room (OR)?
4. What are the special considerations for anesthetic setup in this case?

C. Intraoperative Management

1. What is a laser and how does it work?
2. What are the characteristics of laser radiation?
3. Discuss some advantages associated with the use of lasers for laryngeal surgery.
4. What are some disadvantages of lasers compared with microdebriders?

5. How would you protect the external surface of a conventional endotracheal tube (ETT) for use during laser microlaryngoscopy?
6. What are the disadvantages of foil-wrapped tubes?
7. What special ETTs are available for laser surgery?
8. How would you manage an airway fire?
9. What is the Venturi effect?
10. What is Venturi jet ventilation?
11. How would you institute and conduct manual jet ventilation?
12. How is anesthesia maintained during jet ventilation?
13. What are the complications of jet ventilation?
14. Are there contraindications for the use of jet ventilation?
15. Discuss airway management options during laryngeal papilloma resection.
16. How would you plan to monitor this patient?
17. How would you induce anesthesia for an intermittent apnea technique?

D. Postoperative Management

1. After uneventful laser microlaryngeal resection using jet ventilation, the patient was extubated in the OR and then transferred to the recovery room. What are the common postoperative complications?

A. Medical Disease and Differential Diagnosis

A.1. What is the cause of RRP?

RRP, a disease of the respiratory mucosa characterized by benign nonkeratinizing squamous papillomata, is caused by the human papilloma virus (HPV). On the basis of shared genetic code homologies, HPV are grouped and numbered. Although there are approximately 100 different HPV types identified to date, with respect to RRP, two types stand out: HPV 6 and 11. They are not only the causative agents for RRP but are also responsible for 90% of genital warts (*Condylomata acuminata*). Recently, there has been evidence implicating infections with non-HPV agents in the pathogenesis of RRP.

Derkay CS, Faust RA. Recurrent respiratory papillomatosis. In: Flint PW, Haughey BH, Lund VJ, et al., eds. *Cummings Otolaryngology: Head & Neck Surgery*. 5th ed. Philadelphia: Mosby; 2010:2884–2895.

Donne A, Hampson L, Homer J, et al. The role of HPV type in recurrent respiratory papillomatosis. *Int J Pediatr Otorhinolaryngol*. 2010;74:1:7–14.

A.2. Does delivery through cesarean section prevent infection of the neonate with human papilloma virus (HPV)?

HPV has been estimated to be present in the genital tract of as many as 25% of all women of childbearing age worldwide. Although RRP is the most common benign neoplasm of the larynx in children, its true incidence and prevalence are uncertain. It is estimated that each year, 1,500 to 2,500 new cases of childhood-onset RRP occur in the United States. Therefore, only a minority of children of virus-carrying mothers will become symptomatic, which is not to say that the number of virus-carrying children is not much higher. Even in parturients with an active genital condyloma lesion, the child's risk of contracting the disease when normal spontaneous vaginal delivery is chosen is only approximately 1 in 400.

The route of transmission (i.e., transplacental, perinatal, or postnatal) is not completely understood, as is the preventive value of cesarean sections in parturients known to carry the virus. Cesarean section with the sole intention of preventing the disease in the newborn is therefore not recommended. It may have a role in preventing excessive maternal bleeding likely to result from normal spontaneous vaginal delivery or in circumventing pelvic outlet obstruction secondary to excessive lesions.

It is hoped that with the wider availability of vaccines effective against HPV 6 and 11 (Gardisil, Merck & Co., Inc., Whitehouse Station, NJ), the incidence of RRP will decrease in the future.

Centers for Disease Control and Prevention. *Sexually transmitted disease guidelines*. 2002. Available from: http://www.cdc.gov/STD/treatment/6-2002 TG.htm.

Derkay CS, Faust RA. Recurrent respiratory papillomatosis. In: Flint PW, Haughey BH, Lund VJ, et al., eds. *Cummings Otolaryngology: Head & Neck Surgery*. 5th ed. Philadelphia: Mosby; 2010:2884–2895.

A.3. Is this an unusual presentation for RRP?

Recurrence of voice changes despite repeated surgical interventions is unfortunately not that rare in patients with respiratory papillomatosis. Hoarseness, stridor, and—if severe enough—the development of respiratory distress from airway obstruction are the most consistent signs and symptoms of patients with RRP. Oral, tracheobronchial, and pulmonary involvements also are known to occur.

At present, there is no cure for RRP and no modality that would lead to eradication of the virus from the respiratory mucosa. Local recurrences are therefore to be expected.

Derkay CS, Faust RA. Recurrent respiratory papillomatosis. In: Flint PW, Haughey BH, Lund VJ, et al., eds. *Cummings Otolaryngology: Head & Neck Surgery*. 5th ed. Philadelphia: Mosby; 2010:2884–2895.

A.4. What are the available treatment options for RRP?

As stated in the preceding text, there is no cure but only disease control for relentless and recurrent papillomatosis. The current standard of care is surgical therapy with the goal of complete removal of papillomata and preservation of normal structures as much as possible.

As scarring from overaggressive laryngeal resections may lead to precisely the adverse clinical effects that surgical therapy seeks to avoid or minimize (dysphonia, airway compromise), most experienced surgeons will accept incomplete papilloma resection, especially when near delicate structures such as the anterior laryngeal commissure. Even with the removal of all clinically evident papilloma, not all latent virus particles will have been eradicated.

With respect to surgical technique, the CO_2 laser used to be the mainstay of therapy since the 1970s. According to a recent survey by the American Society of Pediatric Otolaryngology, this may be changing. Most members participating in this survey seem to rely on the use of the microdebrider as the preferred surgical therapy. The microdebrider is considered to be just as precise a surgical tool as the CO_2 laser, while at the same time being easier to use.

There continues to be an appliction for laser-based resections; certain lesions (sessile ones, those with ventricular involvement, or those in the area of significant scarring) still are best dealt with by CO_2-, potassium titanyl phosphate (KTP), or pulsed-dye laser (PDL).

In addition, there seems to be an increasing role for adjuvant medical therapy: α-interferon and various antiviral agents, of which the most commonly used one is intralesional cidofovir.

Derkay CS, Faust RA. Recurrent respiratory papillomatosis. In: Flint PW, Haughey BH, Lund VJ, et al., eds. *Cummings Otolaryngology: Head & Neck Surgery*. 5th ed. Philadelphia: Mosby; 2010: 2884–2895.

Derkay CS, Gallagher TQ. Recurrent respiratory papillomatosis: update 2008. *Curr Opin Otolaryngol Head Neck Surg*. 2008;16:536–542.

Schraff S, Derkay CS, Burke B, et al. American Society of Pediatric Otolaryngology members' experience with recurrent respiratory papillomatosis and the use of adjuvant therapy. *Arch Otolaryngol Head Neck Surg*. 2004;130:1039–1042.

A.5. What are common adverse effects of α-interferon therapy?

Interferons (IFNs) are potent cytokines that possess antiviral, immunomodulating, and antiproliferative activities. Of the three known major classes of IFNs (α, β, and γ), only α-interferon is clinically used in RRP. A common therapeutic regimen entails daily subcutaneous applications for a month, followed by a 6-month period of injections three times a week and then further slow weaning as tolerated. Known adverse effects associated with systemic application are an acute, relatively benign influenza-like syndrome, characterized by fever, chills, headache, myalgia, arthralgia, nausea, vomiting, and diarrhea, as well as more serious dose-limiting comorbidities, namely myelosuppression and neurotoxicity. Neurotoxicity is characterized by somnolence, confusion, behavioral disturbance, and rarely, seizures, debilitating neurasthenia, and depression. Alopecia and personality change are common in IFN-treated children. Cardiovascular toxicity (hypotension and tachycardia) and hepatotoxicity seem to be more rare.

Derkay CS, Faust RA. Recurrent respiratory papillomatosis. In: Flint PW, Haughey BH, Lund VJ, et al., eds. *Cummings Otolaryngology: Head & Neck Surgery*. 5th ed. Philadelphia: Mosby; 2010:2884–2895.

Hayden FG. Chemotherapy of microbial diseases: antiviral agents (nonretroviral). In: Brunton L, Lazo J, Parker K, et al., eds. *Goodman and Gilman's The Pharmacological Basis of Therapeutics*. 11th ed. New York: McGraw Hill; 2005:1243–1273.

A.6. What is the differential diagnosis of hoarseness in this child?

Hoarseness always indicates some abnormality of laryngeal structure or function. Given the patient's previous history, local papilloma recurrence and/or postoperative scarring of laryngeal structures seem likely causes in this patient. A broader differential diagnosis for hoarseness in children would be as follows:

- Anatomic and congenital causes
  - Cystic lesions (laryngocele, thyroglossal cyst)
  - Vocal fold nodules
  - Glottic webs
- Neoplastic causes
  - Squamous cell carcinoma
  - RRP
- Neurologic causes
  - Central (e.g., intracerebral hemorrhage, hydrocephalus)
  - Peripheral neuropathies

- Inflammatory
  - Gastroesophageal reflux
  - Rheumatoid arthritis
  - Angioneurotic edema
- Infectious
  - Croup syndrome
  - Laryngotracheobronchitis
  - Epiglottitis

McMurray JS. Disorders of phonation in children. *Pediatr Clin North Am.* 2003;50:363–380.

B. Preoperative Evaluation and Preparation

B.1. What are the key points of the preanesthetic history and physical examination in this patient?

Of obvious concern in these patients is to quickly detect and address any serious respiratory compromise; in the absence of severe respiratory distress, a detailed history should be obtained. A review of previous anesthetic experiences with particular emphasis on problems pertaining to airway management would be a good starting point. Weight, general health, associated comorbidities, recent respiratory infections, allergies, medications, and nothing-by-mouth status are all of obvious importance. A search for serious adverse effects as a result of the IFN therapy should be done.

With respect to the voice changes, a more in-depth investigation may offer some clues regarding the suspected location: A low-pitched, coarse, fluttering voice suggests a subglottic lesion, whereas a high-pitched, cracking voice, aphonia, or breathy voice suggests a glottic lesion. Associated high-pitched stridor also suggests a glottic or subglottic lesion. Because of the precision of laryngeal mechanics, hoarseness may result from a remarkably small lesion. On the other hand, if the origin of the lesion is remote from the vocal cords, hoarseness may result from a significantly larger lesion.

The concern here is to recognize the lesion that could potentially result in complete airway obstruction once anesthesia has been induced. When in doubt, a flexible nasopharyngoscopy—if not already done before arrival in the operating room (OR)—should be considered immediately preoperatively.

Derkay CS. Recurrent respiratory papillomatosis. *Laryngoscope*. 2001;111:57–69.

B.2. What preoperative laboratory tests are necessary?

In recent years, the value of routine preoperative laboratory screening has been questioned. For a surgical procedure not associated with significant intraoperative blood loss in a child who is not at increased risk for severe and physiologic important anemia, no laboratory tests are required.

This patient may however no longer fall into this latter category. After all, α-interferon is associated with serious side effects, such as neurotoxicity and myelosuppression. Because effects of myelosuppression may not be diagnosed easily by history and physical examination, one might argue that at least obtaining a hematocrit would be in order in this particular patient.

Institute for Clinical Systems Improvement (ICSI). *Preoperative Evaluation*. Bloomington: Institute for Clinical Systems Improvement (ICSI); 2008 Jul:32. [20 references]

National Guideline Clearinghouse. Guideline archive. Available at: http://www.guideline.gov/summary/summary.aspx?ss=15&doc_id=12973&nbr=6682&string

Steward DJ. Preoperative evaluation and preparation for surgery. In: Gregory GA, ed. *Principles of Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 2002:184.

B.3. How should this child be premedicated before coming to the operating room (OR)?

Children with recurrent RRP are often quite anxious and apprehensive coming back to the OR for yet another reexcision. A reassuring preoperative visit by the anesthesiologist should help allay fears. Sedative premedication should be used very carefully, especially in the child with significant respiratory distress. It should not be administered without close monitoring and the immediate availability of oxygen, suction, and positive pressure ventilation. Anticholinergic premedication may be used to dry up oral secretions.

Brett CM, Zwass MS. Eyes, ears, nose, throat and dental surgery. In: Gregory GA, ed. *Principles of Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 2002: 687–688.

B.4. What are the special considerations for anesthetic setup in this case?

Before the initiation of anesthesia, the anesthesiologist should discuss the case with the surgeon. The anesthesiologist should seek a thorough understanding of the surgical plan and must keep in close communication with the surgeon throughout the procedure. A strategy for maintaining oxygenation and ventilation during the case, while working around surgical needs, must be devised. Special equipment (e.g., laser, jet ventilator, bronchoscopes) must be present and in good working condition.

Preparations for successfully dealing with the difficult pediatric airway should be made by both the anesthesia team (difficult airway cart, senior pediatric anesthesiologist) and the surgical team (open tracheotomy set and experienced otolaryngologist on standby).

Whether a laser will be used greatly impacts on airway management. The biggest concern here is prevention of an airway fire. Also, a plan to deal effectively with such a disaster, should it occur, needs to be firmly established beforehand. Aside from that, all OR staff must wear protective eye gear and laser masks when working around the laser.

Derkay CS. Recurrent respiratory papillomatosis. *Laryngoscope*. 2001;111:57–69.

C. Intraoperative Management

C.1. What is a laser and how does it work?

Electromagnetic radiation consists of photons, and photons have properties consistent with both particles and waves. Like radio waves and Roentgen waves, visible light is another form of electromagnetic radiation.

The characteristic features of these different forms of radiation are their respective wavelengths. Visual light is electromagnetic radiation with wavelengths in the range from 385 to 760 nm, shorter wavelengths are ultraviolet, and longer wavelengths are infrared.

Laser is an acronym for light amplification by stimulated emission of radiation. What makes laser special is the high-energy density that it provides, and the ability to quickly transfer large quantities of energy to remote locations, be it through fiberoptic channels (for example with the potassium titanyl phosphate laser) or through free air, as is usually the case with the CO_2 laser.

Several concepts are important for a basic understanding of the phenomenon of laser:

- *The photoelectric effect*. Light of a certain wavelength (e.g., blue) causes metal to eject electrons at a rate proportional to the brightness of this light. Intense light of different colors (e.g., red, orange, yellow) cannot do that.
- *The orbital model*. Electrons circling the nuclei of atoms are limited to a few specific orbital patterns and radii. Each orbital has its specific energy level. The energy differences between electron orbitals are charceteristic for specific atoms. The only way an electron can move from one orbital to another of higher or lower energy is to either absorb or emit an amount of energy equivalent to the difference in energy between the two orbitals.
- *Stimulated absorption*. The process by which a photon's energy is captured by an electron, thereby lifting the electron into a higher energy orbital (the electrons get "excited").
- *Spontaneous emission*. The opposite phenomenon during which an electron drops to a lower orbital, in the process sending out a photon carrying away the excess energy.
- *Population inversion*. Many (as opposed to one single) electrons achieve a higher energy level (higher orbital). Once initiated by a single photon, a chain reaction of stimulated emission sets in (amplification).

The necessary components of a laser system consist of a laser medium (gaseous or solid) containing the atoms whose electrons create the laser light, resonating mirrors to enhance laser efficiency, and an energy source to excite the atoms of the laser medium into generating laser light. An energy source provides the means for obtaining a population inversion of orbital electrons of the laser medium. A pair of axial mirrors permits repeated passes of collimated photons through the medium, allowing maximum amplification by stimulated emission. One of the mirrors is partially transmitting, finally allowing the laser beam to emerge.

Rampil IJ. Anesthesia for laser surgery. In: Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:2405–2418.

C.2. What are the characteristics of laser radiation?

The high-energy density of laser is the result of three characteristics:

- There is a high degree of monochromaticity; that is, other than with ordinary light, the range of wavelengths is very limited.
- Electromagnetic fields of all photons in the laser beam oscillate synchronously in identical phase, a phenomenon called *coherence*, again distinct from ordinary light where the electromagnetic fields are phased randomly.
- Whereas ordinary light beams spread out in all directions from a point source, laser light remains in a narrow collimated beam.

These characteristics allow for a very concentrated energy delivery, often producing heating at a rate of many thousand degrees per second with lasers in current clinical application.

Rampil IJ. Anesthesia for laser surgery. In: Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:2405–2418.

C.3. Discuss some advantages associated with the use of lasers for laryngeal surgery.

With laser light, tissue penetration is mostly a function of wavelength. Long-wavelength laser light, such as that from CO_2 (operating at 10,600 nm), is completely absorbed by water in the first few layers of cells. The thermal effect is therefore largely limited to the point of entry into the target tissue. This results in explosive vaporization of the surface tissue of the target with surprisingly little damage to underlying cells. When coupled to an operating microscope, the laser vaporizes the lesions with precision, causing minimal bleeding and edema, an obvious advantage, especially in small pediatric airways.

As mentioned in section A.4, in certain situations, a laser-based resection technique is the surgical method of choice: Sessile lesions, lesions in scarred areas, and those located near or in the laryngeal ventricle often are treated with PDL. Other than the CO_2 laser, this is a laser with a shorter wavelength that typically *spares* the epithelium, but specifically targets the microvascular supply of the overriding lesion. This has obvious advantages, where the epithelium of one wall is in proximity to epithelium from an opposing wall, such as is the case in the anterior laryngeal commissure. Not denuding the epithelium is beneficial from a functional standpoint, as it should limit fibrotic changes from abutting raw surfaces, that might interfere with the delicate interplay of laryngeal substructures. An added benefit at least in the adult patient population is that the PDL can be used with just topical anesthesia alone (delivery is typically via fiberoptic means), thereby avoiding many of the complicating considerations for laser surgery under general anesthesia.

Derkay CS. Recurrent respiratory papillomatosis. *Laryngoscope*. 2001;111:57–69.

Derkay CS, Gallagher TQ. Recurrent respiratory papillomatosis: update 2008. *Curr Opin Otolaryngol Head Neck Surg*. 2008;16:536–542.

Rampil IJ. Anesthesia for laser surgery. In: Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:2405–2418.

C.4. What are some disadvantages of lasers compared with microdebriders?

There are significant risks associated with the use of laser for laryngeal surgery.

Extra staff is typically required for the safe operation of the laser equipment, adding to the overall cost of the procedure.

Special eye protection for both patient and staff are indispensable, as the powerful laser beam may otherwise cause serious ocular injury. Other body parts need also to be carefully protected from inadvertent laser exposure in order to prevent tissue injury. Inappropriate and aggressive use of the laser may also cause injury to mucosa primarily not affected by disease and create an environment suitable for implantation of viral particles and thereby may actually promote spread of the disease. Laser-induced pneumothorax has been reported after a laryngeal procedure. Although the thermal effect is largely limited to the point of entry into the target tissue, if not used judiciously especially near delicate structures such as the anterior or posterior laryngeal commissure, laser may cause unacceptable scarring and subsequent abnormal vocal fold function.

Laser smoke contains water vapor and destroyed tissue material. It has been found to contain active viral DNA, a potential source of infection for OR personnel. Smoke may also obstruct the surgeon's view during the resection.

The biggest concern with laser use, however, revolves around the generation of an airway fire through ignition of the endotracheal tube (ETT) by inadvertent laser strike, a potentially fatal complication if not effectively dealt with quickly.

When comparing the microdebrider and the CO_2 laser, there is evidence suggesting that removing papillomas using the microdebrider is associated with better

short-term improvement in voice quality, and shorter procedure time, which may ultimately translate to reduced operative cost. Heat-induced scarring of nearby tissues is not a concern, there is no need for circumstantial protection from inadvertent laser strike, and the risk for an airway fire should be no higher than in a standard case.

Derkay CS, Faust RA. Recurrent respiratory papillomatosis. In: Flint PW, Haughey BH, Lund VJ, et al., eds. *Cummings Otolaryngology: Head & Neck Surgery*. 5th ed. Philadelphia: Mosby; 2010:2884–2895.

Derkay CS, Gallagher TQ. Recurrent respiratory papillomatosis: update 2008. *Curr Opin Otolaryngol Head Neck Surg*. 2008;16:536–542.

Pasquale K, Wiatrak B, Woolley A, et al. Microdebrider versus CO_2 laser removal of recurrent respiratory papillomas: a prospective analysis. *Laryngoscope*. 2003;113(1):139–143.

Rampil IJ. Anesthesia for laser surgery. In: Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:2405–2418.

Werkhaven JA. Microlaryngoscopy-airway management with anaesthetic techniques for CO_2 laser. *Pediatr Anesth*. 2004;14:90–94.

C.5. How would you protect the external surface of a conventional endotracheal tube (ETT) for use during laser microlaryngoscopy?

Inadvertent laser strike can ignite and burn any hydrocarbon material in the airway, including ETTs. Because of their proximity to the operative field, ETTs pose a serious fire hazard during laser use, especially in the oxygen-enriched environment of a general anesthetic.

All commonly used ETTs are potentially flammable, but to some degree flammability is a function of the material used to manufacture the tube. Unfortunately, the now commonplace clear polyvinylchloride (PVC) plastic tubes seem to catch fire much more easily than older red rubber tubes. Also, red rubber tubes seem to lead to less toxic combustion products once ignited.

In addition to limiting the amount of oxygen used to ventilate the patient to as low as tolerated, one strategy to make the use of conventional PVC tubes safer is to guard it with reflective tape. Conventional aluminum or copper tape is an inexpensive (although not U.S. Food and Drug Administration [FDA]-approved) way to offer some protection against brief laser strike. FDA-approved tape is also available (Merocel Laser Guard, Medtronic USA).

Should a regular cuffed tube be used, the cuff in itself unfortunately cannot be protected from laser strike in this manner, as it is impractical to wrap the cuff with tape. Cuff breakage needs to be recognized immediately as it increases the fire hazard significantly; it will allow access of oxygen-enriched gas mixtures to the hypopharynx. One strategy here to reduce risk is to fill the cuff with an indicator dye (e.g., methylene blue in normal saline) to detect a break early and hopefully douse small fires at the same time. The cuff should also be covered from above with wet gauze or neurosurgical sponges to retard heating.

To wrap a PVC tube with tape, the tube should be clean and fat-free, thereby facilitating tape adhesion. The tube diameter should be chosen 1 to 2 mm smaller than usual. Mastisol will further enhance the stickiness to the ETT. Wrapping should start at the distal end or just proximal to the cuff and be continued up to the level of the uvula. The distal end of the tape should be cut at a 60-degree angle, and the tube should then be wrapped in a spiral with approximately 30% overlap, avoiding sharp edges and leaving no PVC exposed.

Rampil IJ. Anesthesia for laser surgery. In: Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:2405–2418.

Wöllmer W, Wolfgang W, Schade G, et al. Endotracheal tube fires still happen – a short overview. *Medical Laser Application.* 2010;25:118–125.

C.6. What are the disadvantages of foil-wrapped tubes?

Disadvantages of metallic foil-wrapped tubes include risk of trauma to pharyngeal and laryngeal tissues by sharp edges. The tube will lose elasticity and be more prone to kink. If foil becomes detached, the protective effect is lost and aspirated foil may lead to airway obstruction. The reflective surface enhances the risk of inadvertent laser strike of surrounding tissues.

Brett CM, Zwass MS. Eyes, ears, nose, throat and dental surgery. In: Gregory GA, ed. *Principles of Pediatric Anesthesia.* 4th ed. New York: Churchill Livingstone; 2002:687–688.

Wöllmer W, Wolfgang W, Schade G, et al. Endotracheal tube fires still happen – a short overview. *Med Laser Appl.* 2010;25:118–125.

C.7. What special ETTs are available for laser surgery?

The FDA-approved specialized tubes for laser surgery are commercially available. In essence, there are metal- and silicone-based tubes.

The Xomed Laser Shield and Laser Shield II (Medtronic, USA) are silicone-based tubes with laser-reflective aluminum containing coating or reflective aluminum wrap with smooth fluoroplastic overwrap on the outside (in the case of the Laser Shield II). Although these tubes may withstand laser strikes longer then conventional tubes, they will ignite as well with longer exposure.

Two FDA-approved metal tube models are commercially available for use with CO_2 laser. First, there is the Laser Flex tube (Mallinckrodt, USA), an airtight stainless steel spiral tube with two distal PVC cuffs. If one ruptures, the second unruptured cuff will still limit egress of oxygen-rich gas. Second, the Bivona Fome-Cuf (Bivona, USA) is an aluminum spiral tube with an outer silicone coating. This tube has a specially designed self-inflating foam sponge-filled cuff, which will remain expanded even after laser puncture. Not surprisingly, the rigidity and bulkiness of these tubes are practical disadvantages that discourage from their routine use, especially in pediatric patients. Even with these metal tubes, fire hazard is still a concern.

Green JM, Gonzalez RM, Sonbolian N, et al. The resistance to carbon dioxide laser ignition of a new endotracheal tube: Xomed Laser-Shield II. *J Clin Anesth.* 1992;4(2):89–92.

Rampil IJ. Anesthesia for laser surgery. In: Miller RD, ed. *Miller's Anesthesia.* 7th ed. Philadelphia: Churchill Livingstone; 2010:2405–2418.

Wöllmer W, Wolfgang W, Schade G, et al. Endotracheal tube fires still happen – a short overview. *Med Laser Appl.* 2010;25:118–125.

C.8. How would you manage an airway fire?

In case of an airway fire, rapid and effective action is required. When suddenly faced with this frightening situation, the "4 Es" mnemonic may help you to stay focused:

- *E*xtract
- *E*liminate
- *E*xtinguish
- *E*valuate

All combustible materials (ETT, pledgets) must be *e*xtracted from the airway at once. Oxygen supply through the tube must be quickly *e*liminated by disconnection from the circuit. Continued flow through a burning tube would lead to a blowtorch effect. Any residual fires need to be *e*xtinguished with normal saline. Ventilation with 100% oxygen should then be provided by mask, and anesthesia should be continued. *E*valuation of the injury is then in order and should be done with direct laryngoscopy and rigid bronchoscopy, thereby assessing the upper and lower airway. Any apparent airway damage makes reintubation the most prudent approach. For severe injury, a low tracheotomy may be indicated.

Rampil IJ. Anesthesia for laser surgery. In: Miller RD, ed. *Miller's Anesthesia.* 7th ed. Philadelphia: Churchill Livingstone; 2010:2405–2418.

Werkhaven JA. Microlaryngoscopy-airway management with anaesthetic techniques for CO_2 laser. *Pediatr Anesth.* 2004;14:90–94.

C.9. What is the Venturi effect?

The Venturi effect originally describes the impact of constricted channels on fluid flow. As fluid passes through a constriction of a Venturi tube (a tube with two open ends and a narrowing in its midsection), it must speed up. At the same time, its hydrostatic pressure drops. This pressure drop is proportional to flow, and can, for example, be used to measure flow in pipes without interfering with flow.

Ihra G, Aloy A. On the use of Venturi's principle to describe entrainment during jet ventilation. Letter to the editor. *J Clin Anesth.* 2000;12:417–419.

C.10. What is Venturi jet ventilation?

The jet injector technique of ventilation for upper airway surgery was introduced by Sanders in 1967.

A high-pressure gas source is connected to a stiff, narrow cannula, positioned at the inlet of the laryngoscope. With a manual switch, gas boluses are delivered. In the lumen of the laryngoscope, the high-velocity stream of gas encounters stationary gas, which it pushes forward. Each jet bolus entrains ambient air through the open laryngoscope entrance, substantially augmenting the volume of the bolus and diluting the oxygen fraction of the jet.

Whether or not truly based on the phenomenon known as the *Venturi effect*, the jet injector provides a simple approach to deliver physiologic tidal volumes in a nongas tight delivery system. Venturi ventilation has become synonymous with jet ventilation in the medical literature.

Ihra G, Aloy A. On the use of Venturi's principle to describe entrainment during jet ventilation. Letter to the editor. *J Clin Anesth.* 2000;12:417–419.

McRae K. Anesthesia for airway surgery. *Anesthesiol Clin North America.* 2001;19(3):497–541.

C.11. How would you institute and conduct manual jet ventilation?

Before effective jet ventilation can begin, the operating laryngoscope must be inserted, the larynx adequately exposed and evaluated for appropriateness for jet ventilation, the suspension system installed, and the jet injector needle attached to the laryngoscope and properly aligned with the axis of the trachea. All of this takes time in an anesthetized

apneic patient. Therefore, it is our preference at the New York Presbyterian Hospital-Weill–Cornell Medical Center to begin with laryngoscopy and intubation using a standard PVC ETT if the airway appears appropriate for jet ventilation. Uninterrupted ventilation can now be performed while the operating laryngoscope and jet injector are positioned. When ready, the ETT is removed and jet ventilation begun. Alternatively, following anesthesia induction and demonstration of an adequate mask airway, the patient is paralyzed and the operating laryngoscope and jet injector are inserted and positioned while the patient is apneic.

Ventilation begins with a jet pressure of 5 to 10 psi in infants and children and 15 to 20 psi in adults. The jet pressure is gradually increased until adequate chest excursions are noted. Jet ventilation should produce good clinical expansion of the chest at a rate appropriate for the patient's age. The inspiratory-to-expiratory (I:E) ratio should allow for complete passive exhalation in between jet applications. Monitoring of peripheral arterial saturation is mandatory as is monitoring ventilation both by auscultation and palpation.

Derkay CS, Faust RA. Recurrent respiratory papillomatosis. In: Flint PW, Haughey BH, Lund VJ, et al., eds. *Cummings Otolaryngology: Head & Neck Surgery*. 5th ed. Philadelphia: Mosby; 2010:2884–2895.

Rampil IJ. Anesthesia for laser surgery. In: Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:2405–2418.

C.12. How is anesthesia maintained during jet ventilation?

Because the delivery of inhalational anesthetics is impractical with jet ventilation (OR pollution, inability to precisely regulate their concentrations), most authors favor a total intravenous technique. Combining a hypnotic agent such as propofol with a short-acting opioid (ideally remifentanil), hypnosis, amnesia, and analgesia can all be achieved, while allowing for a rapid recovery of the patient at the end of the procedure. Temporary muscle relaxation can be achieved with either a short-acting or intermediate-duration muscle relaxants.

Patel A, Feldman MA. Anesthesia for eye, ear, nose, and throat surgery. In: Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:2357–2388.

C.13. What are the complications of jet ventilation?

Complications associated with jet ventilation include dehydration of the mucosa, inadequate oxygenation and ventilation, gastric distention, regurgitation, and even rupture. Pneumomediastinum and pneumothorax have been reported, and seem to occur mostly when applying jet ventilation with a (partially) obstructed airway, occurring for example during partial closure of the vocal cords. This is best avoided by using muscle relaxation during jet ventilation.

Borland LM. Airway management for CO_2 laser surgery on the larynx: venturi jet ventilation and alternatives. *Int Anesthesiol Clin*. 1997;35:99–106.

Jaquet Y, Monnier P, Van Melle G, et al. Complications of different ventilation strategies in endoscopic laryngeal surgery. A 10 year review. *Anesthesiology*. 2006;104:52–59.

C.14. Are there contraindications for the use of jet ventilation?

Jet ventilation is most suited for patients with normal, unobstructed airways and normal lung and chest wall compliance.

The ability to fully exhale in between jet applications is crucial. If this is not possible (glottic lesion, significant interarytenoid scarring, laryngospasm), jet ventilation may not be appropriate. Decreased chest wall compliance such as in obese patients may lead to inadvertent gastric distension, further worsening respiratory compliance. Advanced chronic obstructive disease with its inherent prolonged exhalation phase may again make jet ventilation unpractical and in the presence of pulmonary bullae even hazardous. Significant overbite especially when combined with retrognathia makes orolaryngotracheal alignment challenging and accidental gastric hyperinflation likely.

Borland LM. Airway management for CO_2 laser surgery on the larynx: venturi jet ventilation and alternatives. *Int Anesthesiol Clin.* 1997;35:99–106.

Jaquet Y, Monnier P, Van Melle G, et al. Complications of different ventilation strategies in endoscopic laryngeal surgery. A 10 year review. *Anesthesiology.* 2006;104:52–59.

C.15. Discuss airway management options during laryngeal papilloma resection.

In addition to (manual) Venturi jet ventilation, there are three different widely accepted methods for managing the airway during papilloma resection—controlled mechanical ventilation through a small ETT, spontaneous ventilation, and an apnea technique with intermittent ventilation.

Except for the first option, all methods require an at least temporarily unsecured, unprotected airway during parts of the surgical resection. As reassuring as a secured airway may feel to the anesthesiologist, using an ETT during airway laser surgery entails the aforementioned risk of an airway fire. Also, surgical exposure is often suboptimal in the presence of an ETT, as the tube limits access to parts of the larynx.

Access to all parts of the laryngeal mucosa using spontaneous ventilation without an additional airway device (e.g., tube, laryngeal mask airway) is naturally superior. And, depending on the type of laser used, in the *nonpediatric* population, not rarely all that is required is *topical* anesthesia, making it potentially suitable for office-based treatments. In pediatric patients though, maintenance of spontaneous ventilation under general anesthesia is usually the more successful strategy.

For obvious reasons, muscle relaxation is not an option, and the moving surgical field is somewhat of a drawback of this technique, potentially making the resection more demanding.

Intermittent apnea offers a solution to this problem. During apnea with intermittent ventilation, the patient is repeatedly hyperventilated, either by mask or after reintubation. Use of 100% oxygen will extend the tolerable apnea time to follow. Inadvertent movement is best avoided using muscle relaxants. If a tube is used, it is then removed periodically, respirations are held, and the surgeon allowed to operate for brief periods of time, while the peripheral oxygen saturation is closely monitored. The patient is then either reintubated or just masked, before desaturation sets in, and thereby readied for another period of apnea to follow, allowing for further resection as needed. Spreading the virus to more distal parts of the airway by repeated reintubations is a concern with this technique.

Along with spontaneous ventilation, intermittent apnea techniques seem to be favored by most members of the American Society of Pediatric Otolaryngology.

Derkay CS, Faust RA. Recurrent respiratory papillomatosis. In: Flint PW, Haughey BH, Lund VJ, et al., eds. *Cummings Otolaryngology: Head & Neck Surgery*. 5th ed. Philadelphia: Mosby; 2010:2884–2895.

Derkay CS, Gallagher TQ. Recurrent respiratory papillomatosis: update 2008. *Curr Opin Otolaryngol Head Neck Surg.* 2008;16:536–542.

Jaquet Y, Monnier P, Van Melle G, et al. Complications of different ventilation strategies in endoscopic laryngeal surgery. A 10 year review. *Anesthesiology*. 2006;104:52–59.

Schraff S, Derkay CS, Burke B, et al. American Society of Pediatric Otolaryngology members' experience with recurrent respiratory papillomatosis and the use of adjuvant therapy. *Arch Otolaryngol Head Neck Surg*. 2004;130:1039–1042.

C.16. How would you plan to monitor this patient?

Routine monitors include a pulse oximeter, noninvasive blood pressure measurements, an electrocardiogram, a precordial stethoscope, a temperature probe, an oxygen analyzer, a CO_2 detector, and a neuromuscular blockade monitor. In this otherwise healthy patient scheduled for relatively minor surgery without the potential for significant blood loss or fluid shifts, no additional monitoring is necessary.

American Society of Anesthesiologists. http://www.asahq.org/publicationsAndServices/standards/02.pdf

C.17. How would you induce anesthesia for an intermittent apnea technique?

The choice of anesthetic induction is critically dependent upon the presence of signs and symptoms, suggesting possible airway compromise on induction. If those are present, the logical choice in an adult patient is an awake fiberoptic intubation, thereby not only allowing to secure the airway but also enabling evaluation of the subglottic airway before tube placement.

In children and uncooperative adults, an inhalation induction using sevoflurane is the next safest option. Maintenance of spontaneous ventilation is again critical. In this scenario, muscle relaxants are unsafe, until it is clear that the patient can be ventilated and/or intubated. If severe compromise is present, an awake tracheotomy under local anesthesia may be the best means of managing the airway.

Blind techniques (lightwand, blind oral or nasal intubation) cannot be recommended in this setting because they carry the risk of bleeding and loss of the airway with an obstructing lesion.

A word of caution here: Papillomas are dynamic lesions in a sense that they may grow rapidly, thereby questioning the validity of any but the most recent endoscopic airway examinations. Also, the absence of suggestive signs and symptoms does not truly guarantee a patent airway once anesthesia has been induced. Hence, extreme caution in managing these patients is essential.

If the patient has truly no airway compromise, any routine induction technique (intravenous or inhalational) can be used safely.

Patel A, Feldman MA. Anesthesia for eye, ear, nose, and throat surgery: In: Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:2357–2388.

D. Postoperative Management

D.1. After uneventful laser microlaryngeal resection using jet ventilation, the patient was extubated in the OR and then transferred to the recovery room. What are the common postoperative complications?

Laryngeal edema can occur early in the postoperative period and is usually manifested by retractions and inspiratory stridor in the recovery room. After microlaryngeal

surgery, patients may benefit from humidified oxygen, intravenous steroids (e.g., dexamethasone), and racemic epinephrine inhalation. Laryngospasm may develop because of laryngeal hyperactivity. To reduce the incidence of laryngospasm, topical anesthesia to the larynx may be used. If laryngospasm develops postoperatively, it is treated initially with positive pressure ventilation with 100% oxygen. More severe forms of laryngospasm may require the use of small doses of succinylcholine (1/10 of a normal induction dose, i.e., 0.1 mg per kg intravenously). The occurrence of barotrauma with jet ventilation has been described and should be kept in mind. Pulmonary complications as a result of retained secretions and subsequent atelectasis have been reported.

Jaquet Y, Monnier P, Van Melle G, et al. Complications of different ventilation strategies in endoscopic laryngeal surgery. A 10 year review. *Anesthesiology*. 2006;104:52–59.

Patel A, Feldman MA. Anesthesia for eye, ear, nose, and throat surgery: In: Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:2357–2388.

SECTION X

Pediatrics

CHAPTER 36

Tracheoesophageal Fistula

Jacques H. Scharoun

A 12-HOUR-OLD FULL-TERM INFANT weighing 2.5 kg presents with choking and cyanosis during its first feed. Neonatal intensive care unit (NICU) staff is unable to pass a feeding tube into the stomach. The baby also has copious oral secretions. Before birth, polyhydramnios was seen.

A. Pathophysiology and Differential Diagnosis

1. What is the diagnosis? What are the clinical features of this disease?
2. What is the pathophysiology of this disease?
3. How does this lesion occur during development?
4. How are different types of tracheoesophageal fistula (TEF) classified?
5. What other problems may this child have, and when should these be investigated?
6. What should the parents be told regarding perioperative risk? Risk of recurrence?

B. Preoperative Evaluation and Preparation

1. What laboratory workup should be obtained before surgery?
2. What options are there if patient has severe lung disease?
3. Describe management in the NICU before surgery.
4. Should these patients be routinely intubated preoperatively for airway protection?

C. Intraoperative Management

1. What intravenous (IV) access and monitoring are appropriate before induction? After induction?
2. Discuss fluid and temperature management for this baby.
3. What are the options regarding induction and intubation?
4. What is the role of fiberoptic bronchoscopy in this patient?
5. Discuss the surgical technique.
6. Discuss common intraoperative problems for this repair.

D. Postoperative Issues

1. When should the baby be extubated?
2. What pain control options are available?
3. What are early and late complications of TEF repair?

A. Pathophysiology and Differential Diagnosis

A.1. What is the diagnosis? What are the clinical features of this disease?

This patient has esophageal atresia (EA) with TEF. This occurs in 1 per 4,000 live births. The diagnosis is suspected prenatally by the presence of polyhydramnios caused by failure of the fetus to swallow amniotic fluid (secondary to EA). Polyhydramnios can also be caused by other defects, including duodenal atresia, anencephaly, congenital diaphragmatic hernia, and Trisomy 18, and only 10% to 20% of fetuses with polyhydramnios will have other anomalies. There will be an absence of fluid-filled stomach bubble on prenatal ultrasound. After birth, the neonate will have copious drooling. Attempting to feed the baby will result in coughing and cyanosis. An orogastric tube (OGT) will coil up in the upper esophageal pouch rather than pass into the stomach.

Bissonnette B, Dalens B, eds. *Pediatric Anesthesia: Principles and Practice*. 2nd ed. New York: McGraw-Hill; 2002:1016.

Brunicardi FC, Anderson DK, Billiar TR, et al., eds. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:1421.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia: Mosby, Elsevier Science; 2011:575.

Houben CH, Curry JI. Current status of prenatal diagnosis, operative management, and outcome of esophageal atresia/tracheo-esophageal fistula. *Prenatal Diagnosis*. 2008; 28:667–675.

Spitz L. Oesophageal atresia. *Orphanet J Rare Dis*. 2007;2:24.

A.2. What is the pathophysiology of this disease?

In this abnormality, the distal trachea is connected to the lower esophagus through a fistula. This causes three problems. First, inhaled air can bypass the lungs and distend the stomach, which will eventually impede ventilation and cause atelectasis. Second, acidic stomach contents are at continual risk of leaking back into and damaging lung tissue. Third, oral secretions tend to pool in the proximal esophageal pouch resulting in intermittent aspiration, coughing, and cyanosis.

Bissonnette B, Dalens B, eds. *Pediatric Anesthesia: Principles and Practice*. 2nd ed. New York: McGraw-Hill; 2002:1016.

Brunicardi FC, Anderson DK, Billiar TR, et al., eds. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:1421.

Hammer GB. Pediatric thoracic anesthesia. *Anesth Analg*. 2001;92:1449–1464.

A.3. How does this lesion occur during development?

The median ventral diverticulum of the foregut differentiates into a separate esophagus and trachea by the end of the fifth week of gestation. New insights into the embryologic origin of TEF came from rat studies wherein fetal rats exposed to

Adriamycin reliably produce TEF closely resembling the most common version seen in humans. In this model, the lung bud was found to trifurcate instead of normal bifurcation. Two branches became normal lungs with pseudostratified columnar epithelium. The third branch grew caudally until it merged with the distal esophagus. Hence, the fistula came from respiratory tissue. Bolstering this conclusion is the finding that the fistula expresses thyroid transcription factor-1, which is found only in respiratory tissue of the foregut. Human studies also corroborate this finding. Sonic hedgehog (SHH) is a secreted signaling glycoprotein involved in directing differentiation of the foregut and lung. Defective SHH signaling is associated with VACTERL type anomalies (including TEF) in SHH-knockout mice studies. The tissue was surgically obtained from the esophageal pouch and fistula in neonates undergoing repair of TEF. This tissue was then stained to detect SHH. The proximal pouch, but not the fistula, stained positive for SHH. This suggests that the fistula is not an esophageal structure, despite superficial resemblance. However, humans with SHH mutation develop holoprosencephaly, which is not associated with TEF.

Brunicardi FC, Anderson DK, Billiar TR, et al., eds. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:1420.

Crisera CA, Grau JB, Maldonado TS, et al. Defective epithelial-mesenchymal interactions dictate the organogenesis of tracheoesophageal fistula. *Pediatr Surg Int*. 2000;16:256–261.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia: Mosby, Elsevier Science; 2011:575.

Kim JH, Kim PCW, Hui C. The VACTERL association: lesions from the Sonic hedgehog pathway. *Clin Genet*. 2001;59:306–315.

Spilde T, Bhatia A, Ostlie D, et al. A role for Sonic hedgehog signaling in the pathogenesis of human tracheoesophageal fistula. *J Pediatr Surg*. 2003;38(3):465–468.

Spitz L. Oesophageal atresia. *Orphanet J Rare Dis*. 2007;2:24.

A.4. How are different types of tracheoesophageal fistula (TEF) classified?

There are five types of TEF according to the classic Gross classification (Fig. 36.1). Type A is pure EA with no involvement of the respiratory tree; this occurs in 8% of cases. Gross type B has esophageal atresia and a fistula connecting the proximal esophageal pouch to the trachea; this occurs in less than 1%. The most common is type C, with esophageal atresia and fistula linking the distal esophagus to the trachea; this occurs in 75% to 80% of cases. Rarely, type D occurs with two fistula connecting both proximal and distal esophagus to the trachea (2%). Type E, known as an H-type

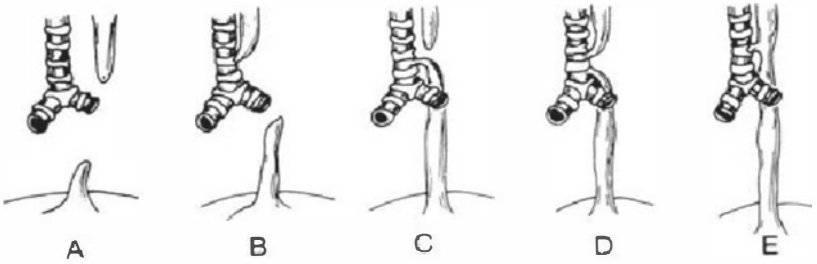

Figure 36.1 Gross's classification of esophageal atresia and tracheoesophageal fistula. (From Gregory GA, ed. *Pediatric Anesthesia*. 2nd ed. New York. Churchill Livingstone, 1989:921, with permission.)

fistula, has no atresia. Instead, an intact esophagus has a linkage with trachea through a fistula, and it occurs in 4%.

Brunicardi FC, Anderson DK, Billiar TR, et al., eds. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:1421.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia: Mosby, Elsevier Science; 2011:575.

A.5. What other problems may this child have, and when should these be investigated?

Unfortunately, TEF often does not occur in isolation. Fifty percent of children with EA/TEF will have additional anomalies. Most often, they occur in the spectrum known as *VACTERL* (formerly known as *VATER*):

V = vertebral anomalies (10%)
A = anal canal defect (anal atresia) (14%)
C = cardiac malformations (29%), including ventricular septal defect, atrial septal defect, tetralogy of Fallot, right sided arch, patent ductus arteriosus)
TE = TEF
R = renal dysplasia
L = limb defect (radial aplasia)

A patient is considered to have VACTERL association with the presence of three or more of these lesions. Nearly one-third of TEF patients will have an additional VACTERL lesion and an additional one-fifth will have two VACTERL problems. Other possible gastrointestinal problems include malrotation of the midgut, and duodenal atresia. Renal problems can include malposition, hydronephrosis, and ureteral abnormalities.

Brunicardi FC, Anderson DK, Billiar TR, et al., eds. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:1421.

Diaz LK, Akpek EA, Dinavahi R, et al. Tracheoesophageal fistula and associated congenital heart disease: implications for anesthetic management and survival. *Pediatr Anesth*. 2005;15:862–869.

Krosnar S, Baxter A. Thoracoscopic repair of esophageal atresia with tracheoesophageal fistula: anesthetic and intensive care management of a series of eight neonates. *Pediatr Anesth*. 2005;15:541–546.

McMullen KP, Karnes PS, Moir CR, et al. Familial recurrence of tracheoesophageal fistula and associated malformations. *Am J Med Genet*. 1996;63:525–528.

Spitz L. Oesophageal atresia. *Orphanet J Rare Dis*. 2007;2:24.

A.6. What should the parents be told regarding perioperative risk? Risk of recurrence?

The survival of TEF babies has improved over the years because of improvements in intensive care unit care, anesthesia, and surgical technique. Waterston developed the first classification of prognosis of TEF in 1962 as follows:

Group A: birth weight greater than 2.5 kg, healthy, survival 95%
Group B: birth weight 1.8 to 2.5 kg and healthy, or greater than 2.5 kg with moderate pneumonia, or other anomalies, survival 68%
Group C: birth weight less than 1.8 kg or greater than 1.8 kg with severe pneumonia or severe congenital anomaly, survival 6%

With improvements in neonatal care, the survival in groups A and B both approach 100%, so new classification systems have been developed to provide more useful information, as birth weight greater than 1.5 kg no longer independently predicts mortality. Of these, perhaps the most useful is the Spitz classification, which is predicated on finding that cardiac disease is the leading risk factor and/or cause of mortality in the TEF group.

Spitz group I: birth weight more than 1.5 kg, no major cardiac disease. Survival 97%
Spitz group II: birth weight less than 1.5 kg, or major cardiac disease. Survival 59%
Spitz group III: birth weight less than 1.5 kg and major cardiac disease. Survival 22%

This date was based on a review of 372 infants from 1980 to 1992. With ongoing improvement in care, a recent review of 188 cases from 1993 to 2004 found Spitz group I survival 99%, group II 82%, and group III 50%.

Most cases of TEF are sporadic, and recurrence rate is 1% in siblings.

Choudhury SR, Ashcraft KW, Sharp RJ, et al. Survival of patients with esophageal atresia: influence of birth weight, cardiac anomaly, and late respiratory complications. *J Pediatr Surg*. 1999;34:70–74.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia: Mosby, Elsevier Science; 2011:574.

Konkin DE, O'Hali WA, Webber EM, et al. Outcomes in esophageal atresia and tracheoesophageal fistula. *J Pediatr Surg*. 2003;38:1726–1729.

Lopez PJ, Keys C, Pierro A, et al. Oesophageal atresia: improved outcome in high-risk groups? *J Pediatr Surg*. 2006;41:331–334.

Spitz L. Oesophageal atresia. *Orphanet J Rare Dis*. 2007;2:24.

B. Preoperative Evaluation and Preparation

B.1. What laboratory workup should be obtained before surgery?

Firstly, one must assess the presence and severity of pulmonary disease, especially looking for aspiration pneumonia, and respiratory distress associated with prematurity. Plain chest x-ray may show infiltrates. It may also show the presence of congestive heart failure in the setting of associated cardiac disease, which may be optimized by administering a diuretic. A radio-opaque OGT will be coiled in the proximal esophageal pouch, whereas an abdominal x-ray may show air in the bowels entering through the fistula. Because of the risk of aspiration, the use of contrast dye to delineate the fistula should be used only when there is diagnostic uncertainty. Ideally, contrast would be given under fluoroscopy, so that any aspiration can be immediately detected. This should only be done if the baby is stable enough to be transported to the fluoroscopy suite. Of note, an OGT that appears to enter the stomach may also reflect esophageal perforation caused by repeated traumatic insertion attempts.

Second, an echocardiogram is *mandatory* as major cardiac defects strongly influence survival and may have an impact on anesthetic management. If the child has severe tetralogy of Fallot, he may require placement of a temporary shunt between the systemic arterial and pulmonary circulation prior to repair of the TEF. In addition, one wants to look for presence of a right-sided aortic arch, because this will require positioning the infant with the opposite side down from usual.

Spinal plain films should be done to exclude vertebral anomalies, especially if epidural pain management is being considered. Renal ultrasound should be done to rule out abnormalities, especially hydronephrosis. In addition, complete blood count

(CBC), arterial blood gas, and electrolytes should be drawn, and at least 1 unit of packed red blood cells should be type and crossed.

Bissonnette B, Dalens B, eds. *Pediatric Anesthesia: Principles and Practice*. 2nd ed. New York: McGraw-Hill; 2002:986, 1017.

Brunicardi FC, Anderson DK, Billiar TR, et al., eds. *Schwartz's Principles of Surgery*, 9th ed. New York: McGraw-Hill; 2010:1422.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia: Mosby, Elsevier Science; 2011:576.

Spitz L. Oesophageal atresia. *Orphanet J Rare Dis*. 2007;2:24.

B.2. What options are there if patient has severe lung disease?

In the past, most children with TEF were routinely given a gastrostomy (under local anesthesia) followed by a staged repair. Beginning in the 80s, this conservative management began to be questioned, and now primary repair is considered standard of care. However, there remains a subset of neonates with severe pneumonia or respiratory distress syndrome, who are considered poor anesthetic and surgical risk (Waterston type C). If the child is intubated because of respiratory disease, one technique to optimize ventilation while minimizing gastric distension (through the fistula) is to employ high frequency oscillator ventilation to minimize the peak inspiratory pressure.

If this is insufficient, a simple gastrostomy is placed to allow drainage of gastric fluid (to minimize further aspiration) and prevent or relieve gastric distension that can occur with positive pressure ventilation (PPV) in the setting of a type C TEF. This procedure can be performed under local anesthesia and obviates the need for a thoracotomy. The problem with this approach is that by decompressing the stomach, gas from the trachea can now bypass the lungs and exit through the stomach. This is especially a concern if the baby's lungs are noncompliant from pneumonia or respiratory distress syndrome. This can make it difficult or impossible to ventilate the baby adequately. Fortunately, this can be alleviated if the gastrostomy tube is placed underneath a water seal therefore allowing gas to escape when it exceeds a predetermined threshold.

More recently, Ratan et al., describe another salvage technique, which involves occluding the fistula retrograde through a gastrostomy. The child is given local anesthetic over the incision site and a styletted no. 10 French Foley catheter is advanced through a gastrostomy to a position just above the gastroesophageal junction using fluoroscopy. The balloon is then inflated and the catheter is either clamped or placed under water seal. In this way the baby could be ventilated with positive pressure while avoiding gastric distention or inadequate ventilation from gas bypassing the lungs. This technique runs the risk of esophageal rupture and fatal pneumothorax if the catheter is not placed properly.

Brunicardi FC, Anderson DK, Billiar TR, et al., eds. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:1422.

Oxford J, Cass DT, Glasson MJ. Advances in the treatment of oesophageal atresia over three decades: the 1970s and the 1990s. *Pediatr Surg Int*. 2004;20:402–407.

Ratan SK, Rattan KN, Ratan J, et al. Temporary transgastric fistula occlusion as salvage procedure in neonates with esophageal atresia with wide distal fistula and moderate to severe pneumonia. *Pediatr Surg Int*. 2005;21:527–531.

Shaul DB, Schwartz MZ, Marr CC, et al. Primary repair without routine gastrostomy is the treatment of choice for neonates with esophageal atresia and tracheoesophageal fistula. *Arch Surg*. 1989;124:1188–1190.

B.3. Describe management in the NICU before surgery.

After diagnosis of TEF is established and other coexisting anomalies investigated, the baby should be immediately placed on NPO (nothing by mouth). He should be kept in a warmed isolette with the head elevated at least 30 degrees to minimize reflux through the fistula. A nasogastric tube should be placed in the proximal esophageal pouch and kept on intermittent suction to minimize aspiration of oral secretions. Antibiotics to treat aspiration pneumonia should be given when appropriate. Ampicillin and gentamicin should be given in those patients who have coexisting significant cardiac disease as prophylaxis. Ensure that blood is available from the blood bank. Because the patient will require a thoracotomy with lung retraction and intermittent compression of the trachea and great vessels, an arterial line is mandatory for the case. This should ideally be placed in the NICU. An umbilical artery line may be conveniently placed by a qualified neonatologist. Two additional IV lines should also be placed, as the patient will be on NPO. Avoid placing lines in the right arm, as this arm will most likely be elevated during right thoracotomy and access will be limited.

Bissonnette B, Dalens B, eds. *Pediatric Anesthesia: Principles and Practice*. 2nd ed. New York: McGraw-Hill; 2002:986, 1017.

Brunicardi FC, Anderson DK, Billiar TR, et al., eds. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:1422.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia: Mosby, Elsevier Science; 2011:576.

Hammer GB. Pediatric thoracic anesthesia. *Anesth Analg*. 2001;92:1449–1464.

B.4. Should these patients be routinely intubated preoperatively for airway protection?

Unless mandated by severe pulmonary disease, the child is not intubated routinely preoperative to minimize the possibility of gastric distension from PPV through the fistula. It is noted that intubation does not protect the child from aspiration of gastric contents through the fistula.

Hammer GB. Pediatric thoracic anesthesia. *Anesth Analg*. 2001;92:1449–1464.

C. Intraoperative Management

C.1. What intravenous (IV) access and monitoring are appropriate before induction? After induction?

At least one peripheral IV should be in place before induction. A second may be placed after the patient is anesthetized. If the surgeon intends to give the child total parenteral nutrition postoperatively, a central line may be placed. Arterial line placement for blood gas and hemodynamic monitoring should be placed before incision if it has not already been inserted in the NICU. If a peripheral A-line is not feasible, an umbilical arterial line may be placed by someone experienced in this technique. Electrocardiogram, oxygen saturation, end-tidal CO_2, and rectal temperature should be also be monitored. A precordial stethoscope should be placed over the left axilla to assess breath sounds in case of inadvertent movement of the endotracheal tube (ETT) during surgical retraction or positioning. A second precordial stethoscope placed over the stomach may be useful to assess if the fistula is being ventilated.

If a gastrostomy tube is present, the end may be placed underneath a water seal. The presence of bubbling indicates ventilation through the fistula, which will occur if the tip of the ETT is proximal to the opening of the fistula. A capnograph inserted into the gastrostomy tube will indicate the same thing.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia: Mosby, Elsevier Science; 2011:577.

C.2. Discuss fluid and temperature management for this baby.

As with all neonates undergoing surgery, meticulous attention to fluid management and temperature is essential. The child should be transported to the operating room (OR) (in a head-up position) in a warmed isolette, with a stocking cap on the head to minimize temperature shifts. The OR should be prewarmed to at least 85°F. Surgical irrigation and IV crystalloid should be warmed, as well as any blood products stored on ice. Using a forced-air convective warming system is strongly recommended. An appropriate size heat-moisture exchanger placed in the airway can be useful. Keep in mind that the neonate is more prone to develop hypothermia for a number of reasons including limited subcutaneous fat. One way the baby compensates is with brown fat nonshivering thermogenesis. When choosing an anesthetic technique, keep in mind that volatile anesthetics including halothane and isoflurane can decrease thermogenesis by up to 70%.

Considering that the patient has been on NPO since birth and whatever was fed probably did not reach the stomach because of esophageal atresia, it is advisable to administer dextrose-containing solution at a controlled rate during the operation. D10/0.2 NS administered IV at maintenance rate using a controlled-infusion pump is an excellent way to avoid hypoglycemia. Insensible losses should be estimated at 3 to 4 mL/kg/hour and replaced with isotonic solution. Urine output (ideally 1 mL/kg/hour) may be difficult to assess accurately in a low–birth weight baby.

Bissonnette B, Dalens B, eds. *Pediatric Anesthesia: Principles and Practice*. 2nd ed. New York: McGraw-Hill; 2002:1003, 1012.

Brunicardi FC, Anderson DK, Billiar TR, et al., eds. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:1422.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia: Mosby, Elsevier Science; 2011:1157.

C.3. What are the options regarding induction and intubation?

The goal is to intubate the baby to allow adequate gas exchange with the lowest possible inspiratory pressure needed to inflate the lungs, avoid atelectasis, and avoid distension of the abdomen. Positive pressure mask ventilation should be avoided. There are several options. First is to keep the child spontaneously ventilating until the fistula is ligated. This requires a deep inhalational technique with gentle assisting of each breath to minimize atelectasis. Intubation can be performed either awake or after inhalation induction. In this way, the lowest inspiratory pressure is required, minimizing distension of the stomach. Awake intubation used to be common, but attention must be paid to the possibility of increased intracranial pressure or intraventricular hemorrhage in the premature infant, as well as the obvious discomfort to the child. Good intubating conditions can be achieved with deep volatile agent, but maintaining adequate ventilation and surgical conditions during a thoracotomy without relaxant may be challenging. Rapid sequence IV induction and intubation (to minimize

face-mask ventilation) is another option provided that attention is paid to minimizing inspiratory pressure.

As important as the intubation is the correct positioning of the ETT. The goal is to have the tip of the ETT distal to the fistula yet proximal to the carina. If the tube is deliberately placed deep (into the right mainstem) with the bevel facing forward, then slowly pulled back just until breath sounds occur on the left equal to the right, the tube is likely to be in good position. If the patient has a preexisting gastrostomy, the ETT should be pulled back almost until gas begins to bubble from the end of the gastric tube (which has been placed under water seal), then readvanced until the bubbling stops. If the tube is in good position, then the child can be paralyzed and normal PPV maintained. The difficulty lies in maintaining good position of the ETT during surgical manipulation and turning the patient lateral.

Andropoulos DB, Rowe RW, Betts JM. Anaesthetic and surgical airway management during tracheoesophageal fistula repair. *Pediatr Anaesth.* 1998;8:313–319.

Bissonnette B, Dalens B, eds. *Pediatric Anesthesia: Principles and Practice.* 2nd ed. New York: McGraw-Hill; 2002:1017.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children.* 8th ed. Philadelphia: Mosby, Elsevier Science; 2011:577.

C.4. What is the role of fiberoptic bronchoscopy in this patient?

Perioperative bronchoscopy before commencing TEF repair has become common. First, the airway can be examined directly to help guide the surgical technique. A cervical level fistula does not require a thoracotomy to repair. Second, if deemed appropriate, the fistula can be occluded using a Fogarty occlusion catheter, thereby allowing unimpeded PPV without distending the abdomen. Bronchoscopy can detect the presence of tracheomalacia, which may assist in planning extubation. Identifying the level of the fistula can assist in correct positioning of the ETT (11% may have it below the carina in one series). Reeves, Burt, and Smith report using a rigid bronchoscope to guide placement of a 2-French Fogarty arterial embolectomy catheter into the TEF and the balloon inflated. The bronchoscope was removed and the patient was then intubated using a 3.0 ETT. Andropoulos, Rowe, and Betts described 61 cases of TEF managed with rigid bronchoscopy. Three babies (those with large fistula) electively had their fistula occluded and all three experience immediate improvement in ventilation. If the fistula was small, it was deemed unlikely to cause ventilatory problems and was left unmodified. Another seven had a catheter placed in the fistula to help the surgeon identify it. This technique of isolating the trachea and esophagus before ligation may be useful in skilled hands. However, there is a real possibility that during positioning or surgical manipulation, the Fogarty balloon may slide back into the trachea. This could precipitate immediate complete airway obstruction if not promptly recognized and treated. Recurrent TEF can be treated endoscopically by placing fibrin glue directly into the fistula, precluding the need for a second thoracotomy.

Andropoulos DB, Rowe RW, Betts JM. Anaesthetic and surgical airway management during tracheoesophageal fistula repair. *Pediatr Anaesth.* 1998;8:313–319.

Meier JD, Sulman CG, Almond PS, et al. Endoscopic management of recurrent congenital tracheoesophageal fistula: a review of techniques and results. *Int J Pediatr Otorhinolaryngol.* 2007;71:691–697.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children.* 8th ed. Philadelphia: Mosby, Elsevier Science; 2011:577.

Reeves ST, Burt N, Smith CD. Is it time to reevaluate the airway management of tracheoesophageal fistula? *Anesth Analg.* 1995;81:866–869.

Veyckemans F, Hamoir M, Rombaux P, et al. Preoperative tracheoscopy in neonates with esophageal atresia (letter). *Anesth Analg.* 2002;96:1827–1828.

C.5. Discuss the surgical technique.

First, the patient is positioned in the lateral position, usually left side down. If the patient has a right-sided aortic arch sometimes the surgeon may wish to position him with right side down. A retropleural approach is used which minimizes the danger from an anastomotic leak. The fistula is exposed and ligated (usually occurs within 45 minutes). The upper esophagus is mobilized, then the distal esophagus. The esophagus is joined together. Following this, a feeding tube is placed across the anastomosis to allow feeding (if the patient does not have a gastrostomy). The lung should be carefully reexpanded to eliminate atelectasis before closure.

Brunicardi FC, Anderson DK, Billiar TR, et al., eds. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:1422–1423.

Houben CH, Curry JI. Current status of prenatal diagnosis, operative management, and outcome of esophageal atresia/tracheo-esophageal fistula. *Prenatal Diagnosis.* 2008; 28:667–675.

Spitz L. Oesophageal atresia. *Orphanet J Rare Dis.* 2007;2:24.

C.6. Discuss common intraoperative problems for this repair.

Interference with ventilation is the most common problem and can have many causes. Lung retraction with resulting atelectasis leads to frequent desaturation. It may be difficult if not impossible to maintain normocarbia. The P_{CO_2} may rise to 70 to 80 mm Hg despite all attempts to optimize ventilation. If the patient has a Fogarty catheter in the fistula, it may be displaced into the trachea causing total airway obstruction. Surgical manipulation of the soft trachea makes it vulnerable to kinking or displacement of ETT distal (into right mainstem) or proximally (above the fistula). Frequent compression of vital structures in the mediastinum can lead to profound hemodynamic compromise. Blood and secretions are a constant problem, which risk obstructing the tube. The ETT should be suctioned frequently, more so if blood is seen. (It does not require much blood to clog a 3.0 ETT.) The retracted lung may need to be intermittently reexpanded to avoid severe hypoxia. Severe gastric distension before ligation of the TEF may require emergent gastric needle decompression. It is crucial to maintain close communication with the surgeon. Avoid hypothermia.

Bissonnette B, Dalens B, eds. *Pediatric Anesthesia: Principles and Practice.* 2nd ed. New York: McGraw-Hill; 2002:1017.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia: Mosby, Elsevier Science; 2011:577.

D. Postoperative Issues

D.1. When should the baby be extubated?

Although some surgeons prefer to have the baby extubated immediately in the OR to minimize tension on the suture line, this can be risky. Many infants with TEF have a

deficiency of tracheal cartilage at the level of the fistula predisposing to tracheomalacia. This can precipitate airway obstruction requiring immediate reintubation. Many of the children have lung disease from prematurity or aspiration pneumonia; after receiving narcotics for pain they may be prone to hypoventilation. If early extubation is planned an epidural technique might be helpful. However, if the child is to remain intubated, care should be made to limit inspiratory pressure to protect the repair from disruption.

Brunicardi FC, Anderson DK, Billiar TR, et al., eds. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:1423.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia: Mosby, Elsevier Science; 2011:578.

Spitz L. Oesophageal atresia. *Orphanet J Rare Dis*. 2007;2:24.

D.2. What pain control options are available?

If the patient is going to remain intubated postoperative (most likely) then a narcotic technique is advisable. Fentanyl at 10 to 20 μg per kg with muscle relaxant will give hemodynamic stability and allow analgesia to be continued in the postoperative period. For experienced practitioners, epidural can also be placed. An epidural catheter threaded through the caudal space can be threaded up to the thoracic dermatomes. Check the placement of the catheter using fluoroscopy before using it. This technique should only be undertaken by someone highly experienced in regional anesthesia for children, with full awareness of the risks and ability to manage complications.

Bissonnette B, Dalens B, eds. *Pediatric Anesthesia: Principles and Practice*. 2nd ed. New York: McGraw-Hill; 2002:549, 1017.

D.3. What are early and late complications of TEF repair?

Early anastomosis leakage occurs in up to 15%. This may require immediate exploration, or managed expectantly. Esophageal dysmotility and gastroesophageal reflux disease are common; the dysmotility may be from abnormal innervation of the distal esophagus, or may be related to vagal nerve injury during the repair. Stricture of the esophageal anastomosis may require repeated dilatations. Tracheomalacia may be evident postoperative, and vocal cord paresis has been reported.

Brunicardi FC, Anderson DK, Billiar TR, et al., eds. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:1423.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia: Mosby, Elsevier Science; 2011:578.

Diaz LK, Akpek EA, Dinavahi R, et al. Tracheoesophageal fistula and associated congenital heart disease: implications for anesthetic management and survival. *Pediatr Anesth*. 2005;15:862–869.

Houben CH, Curry JI. Current status of prenatal diagnosis, operative management, and outcome of esophageal atresia/tracheo-esophageal fistula. *Prenatal Diagnosis*. 2008; 28:667–675.

Spitz L. Oesophageal atresia. *Orphanet J Rare Dis*. 2007;2:24.

CHAPTER 37

Congenital Diaphragmatic Hernia

Fun-Sun F. Yao, David Stein, and John J. Savarese

A FULL-TERM MALE BABY

was born with respiratory distress and cyanosis. Physical examination showed barrel chest and scaphoid abdomen. The breath sounds were absent in the left side of the chest; the heart sounds were best heard in the right side of the chest. Labored respiration, nasal flaring, and sternal retraction were found. The baby weighed 2,800 g. Blood pressure was 60/30 mm Hg; heart rate, 160 beats per minute; respiration, 70 breaths per minute; and temperature, 36° C (96.8° F). Arterial blood gas analysis on room air showed the following: pH, 7.20; $Paco_2$, 55 mm Hg; Pao_2, 35 mm Hg; and CO_2 content, 19 mEq per L.

A. Medical Disease and Differential Diagnosis

1. What differential diagnoses are compatible with these signs and symptoms?
2. Describe the incidence and classification of congenital diaphragmatic hernia (CDH).
3. What are the causes of hypoxemia in patients with CDH?
4. How does the diaphragmatic hernia develop in the fetus? Why do varying degrees of pulmonary hypoplasia usually accompany CDH? How do they affect the prognosis?
5. How do you assess the severity of pulmonary hypoplasia?
6. Discuss persistent pulmonary hypertension (PPH) in the patient with CDH.
7. How do you make a diagnosis of right-to-left shunting through the patent ductus arteriosus or patent foramen ovale?
8. What other congenital anomalies are usually associated with CDH?

B. Preoperative Evaluation and Preparation

1. How would you interpret the following arterial blood gas analyses: pH, 7.20; $Paco_2$, 55 mm Hg; Pao_2, 35 mm Hg; and CO_2 content, 19 mEq per L? How would you correct them?
2. What immediate treatment should be given to improve the newborn's respiratory status preoperatively?

3. Should CDH be repaired urgently once the diagnosis is made and confirmed?
4. How would you treat pulmonary hypertension and improve oxygenation?
5. What are the effects of nitric oxide (NO) on pulmonary and systemic circulation?
6. How is extracorporeal membrane oxygenation (ECMO) established?
7. What are the advantages of ECMO?
8. What are the indications and contraindications to ECMO?
9. When is the optimal time to repair CDH?
10. What other measures should you take to prepare the patient for surgery?
11. How would you premedicate this patient?

C. Intraoperative Management

1. What monitors would you use for this neonate during surgery?
2. How would you induce and maintain anesthesia?
3. Would you use nitrous oxide for anesthesia? Why?
4. Would you use 100% oxygen during anesthesia?
5. How would you ventilate the patient?
6. How would you maintain the neonate's body temperature?
7. The surgeon returned the intrathoracic stomach and intestine to the peritoneal cavity and the ipsilateral lung was found to be hypoplastic and collapsed. The resident anesthesiologist tried to expand the collapsed lung manually with positive airway pressure. Five minutes after the abdomen was closed, the blood pressure suddenly dropped from 70/40 to 30/20 mm Hg, the heart rate from 150 to 80 beats per minute, and the pulse oximeter from 95% down to 60% saturation. What would you do immediately?
8. Discuss fluid therapy in this patient.
9. At the conclusion of surgery, would you extubate the patient in the operating room?

D. Postoperative Management

1. What postoperative problems would you expect in this patient? What is the mortality rate in patients with CDH?
2. The neonate's blood gas analyses improved right after surgery. However, 3 hours later, severe hypoxemia recurred in spite of ventilatory support with high inspired oxygen concentration. What are the possible causes? How should this patient be treated?

A. Medical Disease and Differential Diagnosis

A.1. What differential diagnoses are compatible with these signs and symptoms?

Congenital cardiopulmonary anomalies should be considered whenever cyanosis and respiratory distress are present. A scaphoid abdomen is present due to the absence of abdominal contents. The presence of the barrel chest, bowel sounds in the chest, and the shift of heart sounds to the right definitely suggest the diagnosis of CDH. To confirm the diagnosis, a chest radiograph should be performed to demonstrate gas-filled loops of bowel and probably the spleen or liver in the chest. The lung on the side of the hernia is compressed into the hilum, and the mediastinum is shifted to the opposite side of the chest. If in doubt, a radiopaque dye may be injected through a nasogastric tube to delineate the stomach and intestine in the chest.

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1193–1194.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*, 8th ed. Philadelphia: Mosby, Elsevier Science; 2010:567–574.

Gregory GA, ed. *Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 2002:435.

Hines RL, Marschall KE. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone/Elsevier; 2008:593–594.

Kliegman RM, Behrman RE, Jenson HB, et al., eds. *Nelson's Textbook of Pediatrics*. 18th ed. Philadelphia: Saunders; 2007:746–749.

A.2. Describe the incidence and classification of congenital diaphragmatic hernia (CDH).

The incidence of CDH is estimated to be 1 in 2,500 to 5,000 births. The male/female ratio is 2:1, and the left diaphragm is more frequently involved than the right (5:1).

The diaphragm is embryologically formed from the fusion of several components; therefore, a number of developmental defects may occur, resulting in herniation of abdominal contents into the chest. Embryologically, two fundamental types of defects may occur:

- Complete or partial absence of the diaphragm
- Failure of complete muscularization

Embryologic classification is not convenient clinically. A practical classification is used based on the anatomic location of the defects in the diaphragm:

- *Absent diaphragm*.Very rare
- *Diaphragmatic hernia*. (Fig. 37.1)
  - Posterolateral (Bochdalek): 80%
  - Anterior (Morgagni): 2%
  - Paraesophageal: 15% to 20%
- *Eventration*. Very rare

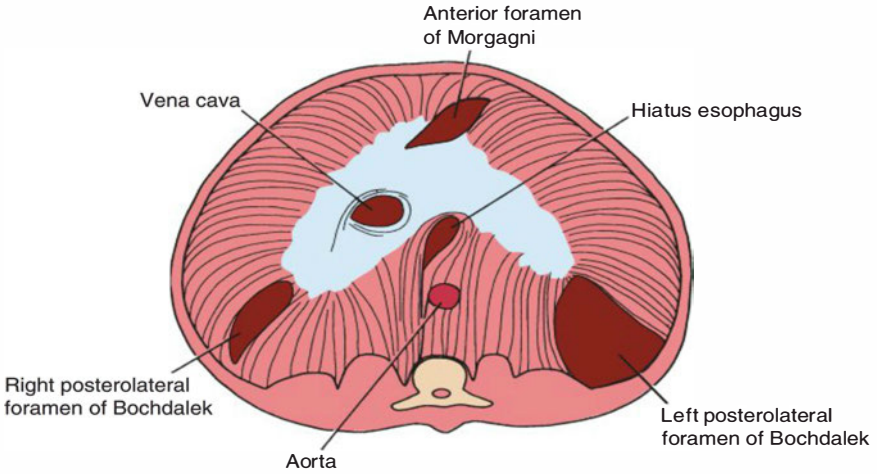

Figure 37.1 Potential sites of congenital diaphragmatic hernia.

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1193–1194.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*, 8th ed. Philadelphia: Mosby, Elsevier Science; 2010:567–574.

Kliegman RM, Behrman RE, Jenson HB, et al., eds. *Nelson's Textbook of Pediatrics*. 18th ed. Philadelphia: Saunders; 2007:746–749.

A.3. What are the causes of hypoxemia in patients with CDH?

The causes of hypoxemia are as follows:

- Atelectasis resulting from compression of the developed lung by the herniated abdominal organs
- Pulmonary hypoplasia with a decrease in the number of alveoli and bronchial generations. The hypoplastic lung will have abnormal pulmonary vasculature resulting from a disruption of normal development of the lung tissue, secondary to the crowding of the herniated abdominal organs in the thorax.
- PPH, causing increased right-to-left shunting through a patent foramen ovale and ductus arteriosus

Gregory GA, ed. *Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 2002:435–436.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*, 8th ed. Philadelphia: Mosby, Elsevier Science; 2010:567–574.

Hines RL, Marschall KE. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone/Elsevier; 2008:593–594.

Kliegman RM, Behrman RE, Jenson HB, et al., eds. *Nelson's Textbook of Pediatrics*. 18th ed. Philadelphia: Saunders; 2007:746–749.

A.4. How does the diaphragmatic hernia develop in the fetus? Why do varying degrees of pulmonary hypoplasia usually accompany CDH? How do they affect the prognosis?

Embryologic development of the diaphragm, gut, heart, and lungs takes place at about the same time, and abnormal development of one organ affects development of the others. Normally, the pleural and peritoneal cavities are separated by the diaphragm from the 8th to the 10th week of gestation. At about the same time, the gut physiologically herniates into the yolk stalk but then returns to the peritoneal cavity. The pleuroperitoneal canals progressively narrow and are finally closed by the 10th week. CDH may result either from the early return of the midgut to the peritoneal cavity or from delayed closure of the pleuroperitoneal canal.

The lung is also undergoing development at this time. Alveolar buds begin to differentiate by the 6th week; airways develop from the 10th to the 12th week. Bronchial branching continues until the 16th week of gestation. Alveolar multiplication continues until 8 years of age.

The degree of pulmonary hypoplasia is related to the timing of the herniation of abdominal organs into the pleural cavity. The earlier the herniation, the more severe the pulmonary hypoplasia. Hypoplasia of the left ventricle may also occur, resulting in cardiac insufficiency. The degree of pulmonary hypoplasia determines the prognosis of CDH. Severe bilateral hypoplasia predicts high mortality. With unilateral hypoplasia, the patient may survive with aggressive therapy. When pulmonary hypoplasia is insignificant, the prognosis is excellent.

Barash PG, Cullen BF, Stoelting RK et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1193–1194.

Berdon WE, Baker DH, Amoury R, et al. The role of pulmonary hypoplasia in the prognosis of newborn infants with diaphragmatic hernia and eventration. *Am J Roentgenol*. 1968; 103:413–421.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*, 8th ed. Philadelphia: Mosby, Elsevier Science; 2010:567–574.

Gregory GA, ed. *Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 2002:435.

Kliegman RM, Behrman RE, Jenson HB, et al., eds. *Nelson's Textbook of Pediatrics*. 18th ed. Philadelphia: Saunders; 2007:746–749.

A.5. How do you assess the severity of pulmonary hypoplasia?

The severity of pulmonary hypoplasia is assessed by the intrapulmonary shunt (Qs/Qt) or the alveolar–arterial difference in oxygen tension (P_{AO_2}–Pa_{O_2}). A (P_{AO_2}–Pa_{O_2}) of more than 500 mm Hg when breathing 100% oxygen is predictive of nonsurvival, and a (P_{AO_2}–Pa_{O_2}) of less than 400 mm Hg is predictive of survival. A (P_{AO_2}–Pa_{O_2}) between 400 and 500 mm Hg represents a zone of uncertain prognosis.

The severity of pulmonary hypoplasia may also be evaluated more aggressively by cardiac catheterization and pulmonary angiogram to define the size and branching pattern of the pulmonary arteries. Patients with severe pulmonary hypoplasia typically will have a fixed right-to-left shunting at the level of the patent ductus arteriosus or patent foramen ovale caused by pulmonary hypertension. Pulmonary angiography demonstrates a small diameter of affected pulmonary artery compared with the main pulmonary artery. The postductal Pa_{O_2} never rises to more than 60 mm Hg in nonsurvivors.

Harrington J, Raphaely RC, Downes JJ, et al. Relationship of alveolar-arterial oxygen tension difference in diaphragmatic hernia of the newborn. *Anesthesiology*. 1982;56:473.

Vacanti JP, Crone RK, Murphy JD, et al. The pulmonary hemodynamic response to perioperative anesthesia in the treatment of high-risk infants with congenital diaphragmatic hernia. *J Pediatr Surg*. 1984;19:672–679.

A.6. Discuss persistent pulmonary hypertension (PPH) in the patient with CDH.

Pulmonary hypertension is one of the major causes of hypoxemia in CDH. There are several causes of pulmonary hypertension in these patients:

- Increased pulmonary vascular resistance and pressure result from a hypoplastic lung.
- The pulmonary vasculature is abnormal, with a decrease in volume and marked increase in muscular mass in the arterioles.
- Right-to-left shunting of oxygen depleted venous blood at the patent foremen ovale and the patent ductus arteriosus. This shunting results in varying degrees of hypoxemia, hypercarbia, and acidosis causing high pulmonary vascular resistance and pressure.

When pulmonary artery pressures are higher than systemic pressures, right-to-left shunting occurs across the ductus, resulting in higher Pa_{O_2} in the upper extremities than in the lower extremities. When right ventricular failure (precipitated by pulmonary hypertension, progressive hypoxemia, and acidosis or by closure of the ductus) increases right atrial pressure to a level higher than the left atrial pressure, right-to-left atrial shunting ensues, producing further hypoxemia. Left ventricular failure from hypoxemia and acidosis induces systemic hypotension, resulting in increased ductal shunting and hypoxemia. A vicious cycle is established. Unless pulmonary artery pressure is decreased, progressive hypoxia and death may ensue.

Barash PG, Cullen BF, Stoelting RK et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1193–1194.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*, 8th ed. Philadelphia: Mosby, Elsevier Science; 2010:567–574.

Gregory GA, ed. *Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 2002:424–425, 435, 887.

Kliegman RM, Behrman RE, Jenson HB, et al., eds. *Nelson's Textbook of Pediatrics*. 18th ed. Philadelphia: Saunders; 2007:746–749.

A.7. How do you make a diagnosis of right-to-left shunting through the patent ductus arteriosus or patent foramen ovale?

If right-to-left shunting occurs through the patent ductus arteriosus, the preductal Pao_2 is at least 15 to 20 mm Hg higher than the postductal value. A right-to-left shunt of 20% is considered "normal" for a newborn infant. If shunting occurs through the patent foramen ovale, the preductal Pao_2 is below the value predicted for 20% shunt. When the degree of preductal shunting is severe, detection of ductal shunting is impossible. Echocardiography with color Doppler, cardiac catheterization, and pulmonary angiography will confirm the diagnosis.

Gregory GA, ed. *Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 2002:1171–1173.

Hines RL, Marschall KE. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone/Elsevier; 2008:593–594.

Nelson NM, Prod'Hom LS, Cherry RB, et al. Pulmonary function in the newborn infant: the alveolar-arterial oxygen gradient. *J Appl Physiol*. 1963;18:534.

A.8. What other congenital anomalies are usually associated with CDH?

The incidence of other congenital anomalies in newborns with CDH is as follows:

- *Cardiovascular system*. 13% to 23%; for example, atrial septal defect, ventricular septal defect, coarctation of aorta, and tetralogy of Fallot
- *Central nervous system*. 28%; for example, spina bifida, hydrocephalus, and acephalus
- *Gastrointestinal system*. 20%; for example, malrotation and atresia
- *Genitourinary system*. 15%; for example, hypospadias

David TJ, Illingworth CA. Diaphragmatic hernia in the southwest of England. *J Med Genet*. 1976;13:253.

Gregory GA, ed. *Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 2002:1171–1173.

B. Preoperative Evaluation and Preparation

B.1. How would you interpret the following arterial blood gas analyses: pH, 7.20; $Paco_2$, 55 mm Hg; Pao_2, 35 mm Hg; and CO_2 content, 19 mEq per L? How would you correct them?

The blood gas analyses showed mixed respiratory and metabolic acidosis and severe hypoxemia. Severe hypoxemia is caused by the pulmonary pathologies and PPH.

Hypoxemia stimulates respiratory chemoreceptors and causes hyperventilation, resulting in respiratory alkalosis initially. However, if hypoxemia is not corrected, the patient will become exhausted and CO_2 retention ensues. Severe pulmonary hypoplasia may also cause CO_2 retention. Severe hypoxemia induces anaerobic metabolism, resulting in lactic acidosis.

Hypoxemia and respiratory acidosis should be treated with mechanical ventilation and oxygen therapy. Metabolic acidosis should be corrected by administration of sodium bicarbonate and improvement of circulation with fluid therapy.

Gregory GA, ed. *Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 2002:435–437.

Hines RL, Marschall KE. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone/Elsevier; 2008:593–594.

Kliegman RM, Behrman RE, Jenson HB, et al., eds. *Nelson's Textbook of Pediatrics*. 18th ed. Philadelphia: Saunders; 2007:746–749.

B.2. What immediate treatment should be given to improve the newborn's respiratory status preoperatively?

Immediate intervention should include decompression of the stomach with an orogastric or nasogastric tube and administration of supplemental oxygen by mask. Positive pressure ventilation by mask should be avoided to prevent distention of the intrathoracic stomach, which will further compress the lung and compromise respiration. If cyanosis and hypoxemia persist, awake intubation should be done to facilitate mechanical ventilation. Positive airway pressure during mechanical ventilation should not exceed 30 cm H_2O to reduce the risk of tension pneumothorax. Although pneumothorax can happen on either side, it occurs more frequently on the contralateral side of the hernia because the pressure needed to expand the hypoplastic lung is higher than that required to rupture the normal lung.

Gregory GA, ed. *Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 2002:435–437.

Hines RL, Marschall KE. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone/Elsevier; 2008:593–594.

Kliegman RM, Behrman RE, Jenson HB, et al., eds. *Nelson's Textbook of Pediatrics*. 18th ed. Philadelphia: Saunders; 2007:746–749.

B.3. Should CDH be repaired urgently once the diagnosis is made and confirmed?

In the past, CDH was considered a surgical emergency, in the belief that the herniated contents caused lung collapse and respiratory failure. However, recognition of the role of pulmonary hypertension, in addition to pulmonary hypoplasia and the effects of surgical repair on pulmonary function, has prompted critical reevaluation of that strategy. It is now clear that lung compression by the herniated viscera is a minor factor in the cardiopulmonary compromise compared with the pulmonary hypertension and hypoplasia. The consensus today is to delay surgery and concentrate on medical stabilization. The goal of preoperative therapy is to reverse the PPH that results in right-to-left shunting across the patent foramen ovale and the ductus arteriosus. Improvement in the infant's status is apparent by improved oxygenation and ventilation. Doppler echocardiography may be used to confirm the decreased pulmonary vascular resistance. The time it takes to stabilize the condition varies from 24 to 48 hours in infants with only mild pulmonary hypertension and hypoplasia up to 7 to 10 days in neonates with severe pulmonary hypertension and hypoplasia.

Barash PG. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1193–1194.

Charlton AJ. The management of congenital diaphragmatic hernia without ECMO. *Paediatr Anaesth*. 1993;3:201.

Gregory GA, ed. *Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 2002:436–437.

Haugen SE, Linker D, Eik-Nes S, et al. Congenital diaphragmatic hernia: determination of the optimal time for operation by echocardiographic monitoring of the pulmonary arterial pressure. *J Pediatr Surg*. 1991;26:560.

Kliegman RM, Behrman RE, Jenson HB, et al., eds. *Nelson's Textbook of Pediatrics*. 18th ed. Philadelphia: Saunders; 2007:746–749.

B.4. How would you treat pulmonary hypertension and improve oxygenation?

Pulmonary vascular resistance is greatly increased in the hypoplastic lung, and blood flow is minimal because of medial hyperplasia of pulmonary arterioles. When further aggravated by hypoxemia, acidosis, decreased F_{IO_2}, or sudden changes in pulmonary blood volume, pulmonary vasoconstriction increases and fetal circulation persists. The treatment of pulmonary hypertension includes the following measures in sequence:

- Continue general anesthesia in the intensive care unit, using fentanyl 3 μg/kg/hour, and pancuronium 0.1 mg/kg/hour to blunt the autonomically mediated cardiovascular response (pulmonary vasoconstriction) to stimulation.
- Minimize endotracheal suctioning to avoid transient hypoxemia or decrease in F_{IO_2}.
- Hyperventilate the neonate with low tidal volume and high respiratory rate (60 to 120 breaths/minute) to pH of 7.55 to 7.60. Respiratory alkalosis is the most consistently effective therapeutic modality to achieve pulmonary vasodilation.
- Moderately restrict fluid to 2 to 4 mL/kg/hour.
- Administer pharmacologic vasodilators if the aforementioned measures fail to control pulmonary hypertension. Morphine, prednisolone, chlorpromazine, phentolamine, acetylcholine, bradykinin, tolazoline, prostaglandin E_1, prostaglandin D_2, and inhaled NO have been tried with some success. Milrinone would be helpful if right ventricular failure is apparent.
- Ligate the patent ductus arteriosus to prevent shunting. This is theoretically possible but practically has been associated with sudden right ventricular failure.
- Support with ECMO if pharmacologic intervention fails. ECMO has been associated with a 50% to 65% survival rate.

Barash PG, Cullen BF, Stoelting RK et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1193–1194.

Gregory GA, ed. *Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 2002:436–437.

Vacanti JP, Crone RK, Murphy JD, et al. The pulmonary hemodynamic response to perioperative anesthesia in the treatment of high-risk infants with congenital diaphragmatic hernia. *J Pediatr Surg*. 1984;19:672–679.

B.5. What are the effects of nitric oxide (NO) on pulmonary and systemic circulation?

When produced in vivo, NO is endothelium-derived relaxing factor producing smooth muscle relaxation and vasodilation. Inhaled NO is unique, as it is a selective pulmonary vasodilator and has no effect on systemic circulation because it is

inactivated immediately on exposure to hemoglobin. Clinical studies are limited but have shown some improvement in oxygenation in neonates with PPH exposed to 20 to 80 parts per million (ppm) of NO. NO has been reported to be ineffective before ECMO therapy in those patients with both CDH and pulmonary hypoplasia. After ECMO followed by surgery, NO was effective in improving oxygenation. However, NO has not been shown to improve survival.

Charlton AJ. The management of congenital diaphragmatic hernia without ECMO. *Paediatr Anaesth.* 1993;3:201.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*, 8th ed. Philadelphia: Mosby, Elsevier Science, 2010:567–574.

Gregory GA, ed. *Pediatric Anesthesia.* 4th ed. New York: Churchill Livingstone; 2002:436–437.

Kliegman RM, Behrman RE, Jenson HB, et al., eds. *Nelson's Textbook of Pediatrics*. 18th ed. Philadelphia: Saunders; 2007:746–749.

Wheeler M. Practical anesthetic management of neonatal surgical emergencies. *ASA annual meeting refresher course lectures.* Park Ridge: American Society of Anesthesiologists; 2001:116.

B.6. How is extracorporeal membrane oxygenation (ECMO) established?

Venovenous or venoarterial bypass is used. Venovenous bypass is established with a double-lumen catheter through the internal jugular vein, with blood removed from and infused into the right atrium through separate ports. Venoarterial bypass is used preferentially by some centers because it provides the cardiac support that is often needed. The right atrium is cannulated through the internal jugular vein. Blood is allowed to passively flow by gravity into the ECMO circuit, where it is pumped with an occlusive blood pump into the membrane oxygenator. From the oxygenator, blood is returned through a catheter placed through the right common carotid artery into the ascending aorta.

Gregory GA, ed. *Pediatric Anesthesia.* 4th ed. New York: Churchill Livingstone; 2002:436–437.

B.7. What are the advantages of ECMO?

The theoretical advantages are as follows:

- Diversion of as much as 80% of cardiac output from the right atrium into the extracorporeal circuit immediately reduces or eliminates right-to-left shunting through the foramen ovale or ductus arteriosus.
- Right ventricular work is decreased because of reduced pulmonary blood flow and pressure.
- Pulmonary vasoconstriction is reduced because hypoxemia and acidosis are corrected by ECMO. Improved systemic oxygenation and reduced ductal blood flow may lead to spontaneous closure of the ductus arteriosus.
- The hypoplastic lung is allowed to grow rapidly and alveolar size is increased.
- The incidence of bronchopulmonary dysplasia is reduced because F_{IO_2} and airway pressure are lowered by ECMO.

Gregory GA, ed. *Pediatric Anesthesia.* 4th ed. New York: Churchill Livingstone; 2002:437–438.

B.8. What are the indications and contraindications to ECMO?

Patients with severe hypoxemia, hypercarbia, and pulmonary hypertension who do not respond to maximal conventional respiratory and pharmacologic intervention are candidates for ECMO. However, due to the necessity for anticoagulation and the consumption and inactivation of platelets, ECMO is associated with serious complications of intracranial and pulmonary hemorrhage. The entry criteria include a gestational age of 34 weeks or greater, the presence of a reversible disease process, a minimal weight of 2,000 g, and a predicted mortality of greater than 80%. (Predicted mortality is commonly estimated by the oxygenation index [$FIO_2 \times$ mean airway pressure $\times$ 100/PaO_2].) Values of oxygenation index in excess of 40 predict mortality greater than 80%.

The contraindications to ECMO include the following:

- Gestational age less than 34 weeks
- Weight less than 2,000 g
- Preexisting grade II or greater intracranial hemorrhage
- Congenital or neurologic abnormalities incompatible with good outcome
- More than 1 week of aggressive respiratory therapy
- Congenital heart disease

Dilley RE, Zwischenberger JB, Andrews AF, et al. Intracranial hemorrhage during extracorporeal membrane oxygenator in neonates. *Pediatrics*. 1986;78:699.

Gregory GA, ed. *Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 2002:438–439.

Redmond CR, Goldsmith JP, Sharp MJ, et al. Extracorporeal membrane oxygenation for neonates. *J La State Med Soc*. 1986;138:40.

Stolar CJ, Snedecor SS, Bartlett RH. Extracorporeal membrane oxygenation and neonatal respiratory failure: experience from the extracorporeal life support organization. *J Pediatr Surg*. 1991;26:563.

B.9. When is the optimal time to repair CDH?

The newborn should be maintained on ECMO until the pulmonary hypertension is reversed and improvement in lung function is evident. Doppler echocardiography may be used to confirm the reversal of PPH. This is usually seen within 7 to 10 days but in some infants is not apparent for up to 3 weeks. Newborns who do not demonstrate significant improvement over this time have pulmonary hypoplasia that will not benefit from further extracorporeal life support. Timing of repair of the CDH on ECMO is controversial. Some centers prefer early repair to allow a greater duration of postrepair ECMO, whereas many centers defer repair until the infant has demonstrated the ability to tolerate weaning from ECMO support.

Gregory GA, ed. *Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 1994:436–437.

Haugen SE, Linker D, Eik-Nes S, et al. Congenital diaphragmatic hernia: determination of the optimal time for operation by echocardiographic monitoring of the pulmonary arterial pressure. *J Pediatr Surg*. 1991;26:560.

Kliegman RM, Behrman RE, Jenson HB, et al., eds. *Nelson's Textbook of Pediatrics*. 18th ed. Philadelphia: Saunders; 2007:746–749.

B.10. What other measures should you take to prepare the patient for surgery?

The patient should be examined carefully for the presence and severity of associated congenital anomalies as described in section A.8. Those patients with congenital heart disease in addition to CDH have significantly increased mortality.

Hypothermia should be prevented and corrected. Hypothermia can aggravate the hypoxemia and acidosis. Hypothermia can also lead to coagulopathy and arrhythmia. The neonate should be maintained in a neutral thermal environment of 36.5° to 37.5° C (97.7° to 99.5° F).

Laboratory studies should include arterial blood gases, complete blood cell count, electrolytes, blood sugar, blood type, and cross-match for blood products.

Venous access should be ready before surgery. Peripheral veins in the upper extremities are preferred because reduction of the hernia often increases abdominal pressure and partially obstructs the inferior vena cava, making lower extremity veins less reliable. Neck veins are avoided in case ECMO is required. Central venous access should be attempted through the umbilical or femoral vein.

B.11. How would you premedicate this patient?

No premedication should be given to the neonate with CDH. The newborn should not have any anxiety, and sedatives will further depress the already compromised cardiopulmonary function.

C. Intraoperative Management

C.1. What monitors would you use for this neonate during surgery?

Respiratory

- Precordial and esophageal stethoscope
- Two pulse oximeters, for preductal and postductal oxygen saturation
- Capnometry
- Inspiratory pressure measurement
- Inspiratory oxygen concentration
- Intraoperative arterial blood gas analysis

Cardiovascular

- Five-lead electrocardiogram
- Blood pressure cuff
- Precordial stethoscope
- Arterial line: right radial artery for preductal Pao_2
- Central venous pressure (CVP) line for evaluating volume status and right ventricular performance

Thermoregulatory

- Esophageal or rectal temperature probe

C.2. How would you induce and maintain anesthesia?

If the neonate has not been intubated, intubation should be performed with spontaneous ventilation. Positive pressure ventilation should be avoided before intubation to prevent gastric distention and further compromise of respiration. An awake intubation can be performed after preoxygenation. However, if the neonate is too vigorous for awake intubation, he can be intubated without a muscle relaxant after breathing sevoflurane and oxygen spontaneously.

The choice of maintenance anesthetics depends on the severity of cardiovascular dysfunction. Patients in shock and severe hypoxemia may tolerate only oxygen and a nondepolarizing relaxant such as rocuronium or vecuronium. If blood pressure is adequate and stable, inhalation agents and narcotics in addition to a muscle relaxant, may be titrated to maintain anesthesia. Narcotics and nondepolarizers may be

continued postoperatively to control ventilation and minimize hormonal response to stress, which may increase pulmonary hypertension.

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1193–1194.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*, 8th ed. Philadelphia: Mosby, Elsevier Science; 2010:567–574.

Dierdorf SF, Krichna G. Anesthetic management of neonatal surgical emergencies. *Anesth Analg*. 1981;60:204–214.

Gregory GA, ed. *Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 2002:437.

C.3. Would you use nitrous oxide for anesthesia? Why?

No. Nitrous oxide should not be used in patients with CDH before hernia reduction and abdominal closure. Because nitrous oxide has a higher diffusion capacity than nitrogen (35:1), the amount of nitrous oxide diffused from blood to the gut is much more than the amount of nitrogen diffused from the gut to the blood. Therefore, nitrous oxide may distend the intrathoracic gut and compress the functioning lung tissue, further compromising pulmonary function. Moreover, a distended gut may cause difficulty in abdominal closure and may increase abdominal pressure, compressing the inferior vena cava and resulting in hypotension.

Barash PG. *Clinical Anesthesia*. 6th ed. Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins; 2009:1193–1194.

Eger El II, Saidman LJ. Hazards of nitrous oxide anesthesia in bowel obstruction and pneumothorax. *Anesthesiology*. 1975;26:61.

Fink R. Diffusion anoxia. *Anesthesiology* 1955;16:511–519.

Gregory GA, ed. *Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 2002:437.

C.4. Would you use 100% oxygen during anesthesia?

Selection of the appropriate inspired concentration of oxygen depends on the severity of pulmonary dysfunction. Retrolental fibroplasia (retinopathy of prematurity) is a potential danger during neonatal anesthesia. Current guidelines suggest that infants are at risk for retrolental fibroplasia until 44 to 50 weeks of gestational age. However, hypoxia causes pulmonary vasoconstriction and pulmonary hypertension, which may increase right-to-left shunting of desaturated blood at preductal or ductal level. Serial arterial blood gases may be used to determine the optimal F_{IO_2}. Air is added to oxygen if the Pa_{O_2} on 100% oxygen is more than 90 to 100 mm Hg. The Pa_{O_2} should be optimally kept at 80 to 100 mm Hg or the arterial oxygen saturation between 95% and 98%.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*, 8th ed. Philadelphia: Mosby, Elsevier Science; 2010:567–574.

Dierdorf SF, Krishna G. Anesthetic management of neonatal surgical emergencies. *Anesth Analg*. 1981;60:204–214.

Gregory GA, ed. *Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 2002:436–437.

C.5. How would you ventilate the patient?

Ventilation is controlled either manually or by a respirator. Small tidal volumes should be used to keep the airway pressure below 30 cm H_2O to prevent contralateral

pneumothorax. High respiratory rates (60 to 120 breaths/minute) should be adjusted to achieve hyperventilation to a $Paco_2$ between 25 and 30 mm Hg to lower pulmonary vascular resistance and minimize right-to-left shunting through the patent ductus arteriosus.

Bray RJ. Congenital diaphragmatic hernia. *Anesthesia.* 1979;34:567.

Gregory GA, ed. *Pediatric Anesthesia.* 4th ed. New York: Churchill Livingstone; 2002:436–437.

C.6. How would you maintain the neonate's body temperature?

The neonate is particularly susceptible to heat loss because of a large surface to volume ratio, lack of insulating fat, and a naturally flaccid and open posture. Body temperature should be monitored carefully and maintained within the normal range. The following steps are used to maintain body temperature:

- Warm the operating room to 80.6° F (27° C).
- Use radiant warming lamps and a heating blanket.
- Use a Heat Moisture Exchanger on the ventilator circuit.
- Warm transfused blood and intravenous fluid to 37° C (99.5° F).

Dierdorf SF, Krishna G. Anesthetic management of neonatal surgical emergencies. *Anesth Analg.* 1981;60:204–214.

Gregory GA, ed. *Pediatric Anesthesia.* 4th ed. New York: Churchill Livingstone; 2002:430–437.

C.7. The surgeon returned the intrathoracic stomach and intestine to the peritoneal cavity and the ipsilateral lung was found to be hypoplastic and collapsed. The resident anesthesiologist tried to expand the collapsed lung manually with positive airway pressure. Five minutes after the abdomen was closed, the blood pressure suddenly dropped from 70/40 to 30/20 mm Hg, the heart rate from 150 to 80 beats per minute, and the pulse oximeter from 95% down to 60% saturation. What would you do immediately?

Any sudden deterioration in blood pressure, heart rate, oxygen saturation, or pulmonary compliance is suggestive of tension pneumothorax. Auscultation of the chest, particularly the contralateral side, should be done immediately. If absent or diminished breath sounds confirm the diagnosis, a chest tube should be inserted immediately. A large-bore intravenous catheter with needle may be inserted to release the tension pneumothorax if a chest tube is not immediately available.

The tension pneumothorax is usually on the contralateral side, because the high airway pressure required to inflate the hypoplastic lung may rupture the normal alveoli on the contralateral side, resulting in pneumothorax. Moreover, the ipsilateral chest usually already has a chest tube after surgery.

If there is no pneumothorax, or if deterioration is not improved after insertion of a chest tube, inferior vena cava compression (causing decreased venous return and decreased cardiac output) should be considered. The peritoneal cavity is often underdeveloped and unable to fully accommodate the returned abdominal organs, which increases the intra-abdominal pressure. In this circumstance, the abdominal wound should be opened to relieve the compression on the vena cava and diaphragm. A Silastic patch may be used to cover the abdominal defect temporarily and the defect will be closed at a later time.

Gregory GA, ed. *Pediatric Anesthesia.* 4th ed. New York: Churchill Livingstone; 2002:437.

C.8. Discuss fluid therapy in this patient.

Fluid therapy should be aimed to correct the preoperative deficit, provide maintenance fluid, and replace intraoperative evaporative, third space, and blood losses.

Kidneys are 80% to 90% mature by 1 month of age. Before that time, the infant cannot tolerate the extremes of renal stress. Neonates are obligate sodium losers; therefore, exogenous sodium should be supplied. In addition, neonates have decreased glycogen storage and are prone to hypoglycemia after brief periods of starvation. Therefore, glucose should also be provided. However, hyperglycemia may predispose the patient to intracranial hemorrhage and should be avoided. The preoperative fluid deficit may be evaluated by careful history taking, signs and symptoms of dehydration, urine output, and CVP monitoring. Maintenance fluids consisting of 5% dextrose in one-fourth to one-half strength saline are given at 4 mL/kg/hour. Intraoperative evaporative and third space losses are replaced with Ringer's lactate or saline at approximately 6 to 8 mL/kg/hour. Each milliliter of blood loss is replaced with 3 mL of Ringer's lactate or 1 mL of 5% albumin. Blood pressure, heart rate, urine output, CVP, hematocrit, and sodium and glucose levels are monitored following the fluid therapy.

Dierdorf SF, Krishna G. Anesthetic management of neonatal surgical emergencies. *Anesth Analg*. 1981;60:204–214.

Hines RL, Marschall KE. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone/Elsevier; 2008:593–594.

C.9. At the conclusion of surgery, would you extubate the patient in the operating room?

No. The patient should not be extubated in the operating room because varying degrees of pulmonary dysfunction are always present postoperatively. The endotracheal tube should be left in place and the baby should be transported to the intensive care unit for further postoperative care.

D. Postoperative Management

D.1. What postoperative problems would you expect in this patient? What is the mortality rate in patients with CDH?

The postoperative course is often characterized by a "honeymoon" period of rapid improvement, followed by sudden deterioration with profound arterial hypoxemia, hypercapnia, and acidosis.

The mortality in patients with CDH varies from 30% to 60%. Factors affecting the mortality include the following:

- Pulmonary hypoplasia
- *Associated congenital defect*. Cardiovascular and central nervous systems
- *Inadequate preoperative preparation*. Hypothermia, acidosis, shock, and tension pneumothorax
- *Ineffective postoperative management*. Hemorrhage, tension pneumothorax, inferior vena cava compression, persistent fetal circulation, excessive suction on chest tube

Kliegman RM, Behrman RE, Jenson HB, et al., eds. *Nelson's Textbook of Pediatrics*. 18th ed. Philadelphia: Saunders; 2007:746–749.

Vacanti JP, Crone RK, Murphy JD, et al. The pulmonary hemodynamic response to perioperative anesthesia in the treatment of high-risk infants with congenital diaphragmatic hernia. *J Pediatr Surg*. 1984;19:672–679.

Waldschmidt J, vonLengerke HG, Berlien P. Causes of death in operated neonates with diaphragmatic defects. *Prog Pediatr Surg*. 1979;13:239.

D.2. The neonate's blood gas analyses improved right after surgery. However, 3 hours later, severe hypoxemia recurred in spite of ventilatory support with high inspired oxygen concentration. What are the possible causes? How should this patient be treated?

As discussed earlier, a tension pneumothorax should be considered and treated if it exists. In the absence of a tension pneumothorax, persistent hypoxemia suggests PPH with right-to-left shunting of venous blood. Recurrent pulmonary hypertension carries a high mortality. ECMO support should be continued or reestablished if already discontinued before surgery. If the infant cannot be weaned from ECMO after repair, options include discontinuing support or therapies such as NO or lung transplantation. High-frequency jet ventilation and oscillatory ventilation have had limited success in patients with CDH.

Gregory GA, ed. *Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 2002:437–438.

Kliegman RM, Behrman RE, Jenson HB, et al., eds. *Nelson's Textbook of Pediatrics*. 18th ed. Philadelphia: Saunders; 2007:746–749.

CHAPTER 38

Tetralogy of Fallot

JAMES A. DINARDO

A 5-MONTH-OLD INFANT

recently adopted from South America is being evaluated for stable persistent cyanosis with arterial oxygen saturation (Sao_2) of 70% to 80% since birth. She feeds well and is in the 70th percentile for weight (6.5 kg). An echocardiogram done before her arrival at your institution suggests that she has tetralogy of Fallot (TOF). Although she has never been noted to have a "Tet spell," her Sao_2 was noted to decrease to 60% during a recent febrile episode. Repeat echocardiogram reveals TOF with severe valvular pulmonary stenosis (PS) and mild subvalvular PS secondary to anterior deviation of the conal septum into the right ventricle outflow tract (RVOT). There is a peak instantaneous gradient of 70 mm Hg across the RVOT as determined by continuous wave Doppler.

A. Medical Disease and Differential Diagnosis

1. What is tetralogy of Fallot (TOF)?
2. What is the pathophysiology of TOF with pulmonary stenosis (TOF/PS)?
3. What is shunting and how is $Q_P : Q_S$ calculated?
4. What is the pathophysiology of TOF with pulmonary atresia?
5. How is the arterial O_2 saturation determined in single ventricle physiology?
6. What is a "pink Tet"?
7. What are hypercyanotic spells? How are they treated?
8. What palliative surgical procedures are available for treating this patient with TOF/PS?
9. What definite surgical procedures are available for treating this patient with TOF/PS?
10. What palliative and definite surgical procedures are available for treating a patient with TOF with pulmonary atresia?

B. Preoperative Evaluation and Preparation

1. What preoperative history and physical examination information do you want?
2. Which other abnormalities need to be considered in this patient?
3. In general, what nothing by mouth (NPO) guidelines will you follow and what premedication will you give to a child with congenital heart disease?

C. Intraoperative Management

1. How will you induce anesthesia in this patient if intravenous (IV) access cannot be obtained?
2. Why would end-tidal carbon dioxide ($ETCO_2$) monitoring be of particular use in a patient with TOF/PS?
3. What is near-infrared spectroscopy (NIRS) and what does it measure?
4. What are the important management issues during creation of a palliative shunt?
5. What is the effect of inhalation anesthetics on airway reflexes, myocardial contractility, systemic vascular resistance (SVR), and pulmonary vascular resistance (PVR) in children?
6. What are the pre–cardiopulmonary bypass (CPB) anesthetic goals for a patient undergoing definitive surgical correction of TOF/PS?
7. What interventions will reliably reduce PVR?
8. How does heparin administration and activated coagulation time (ACT) monitoring differ in children as compared with adults?
9. How is heparin reversed?
10. What is the incidence of protamine reactions in children?
11. What is the role of transesophageal echocardiography (TEE) in this patient?
12. What effect would a residual ventricular septal defect (VSD) have in this patient following separation from CPB?

D. Postoperative Management

1. How should postoperative ventilation be managed in this patient following placement of a transannular patch for TOF/PS?
2. Following complete repair of TOF/PS in an infant, what arterial oxygen saturation (Sao_2) is acceptable?
3. Following placement of a modified Blalock-Taussig shunt (MBTS) for TOF/PS in an infant, what Sao_2 is acceptable?
4. What is junctional ectopic tachycardia (JET)?

A. Medical Disease and Differential Diagnosis

A.1. What is tetralogy of Fallot (TOF)?

In 1888, Fallot described a congenital heart defect composed of four characteristics (1) large VSD, (2) right ventricular (RV) outflow obstruction, (3) overriding aorta, and (4) right ventricle hypertrophy (RVH). Broadly defined, TOF is a complex of anatomic malformations consisting of a large malalignment conoventricular VSD, a rightward and anterior displacement of the aorta such that it overrides the VSD, and a variable degree of subvalvular RVOT obstruction due to anterior, superior, and leftward deviation of the conal (infundibular) ventricular septum. In addition, abnormalities in the septal and parietal bands of the crista supraventricularis further exacerbate infundibular obstruction. RVH is the result of chronic RVOT obstruction. The most common associated lesion is a right aortic arch with mirror image arch vessel branching (innominate artery gives rise to left carotid and left subclavian arteries; right

carotid and right subclavian arise separately) present in 25% of patients. Two broad subsets of TOF exist: TOF with PS (TOF/PS) and TOF with pulmonary atresia. A third much less common type of TOF known as *TOF with absent pulmonary valve* will not be considered here.

Tetralogy of Fallot with pulmonary stenosis

TOF/PS involves the features of TOF in conjunction with varying degrees of valvular PS. At one end of the spectrum of TOF/PS the pulmonary valve may be mildly hypoplastic (reduced annulus size) with minimal fusion of the pulmonary valve leaflets (Fig. 38.1). The pulmonary valve is almost always bileaflet. At the other end of the spectrum, the pulmonary annulus may be very small with near fusion of the valve leaflets. It is important to point out that the valvular obstruction is a *fixed* obstruction while the subvalvular obstruction is *dynamic*. Left uncorrected, RVOT obstruction from both valvular and subvalvular obstruction begets progression of subvalvular obstruction as compensatory RVH increases the mass of the RV and infundibulum. The anatomy of TOF/PS can almost always be definitively delineated (including coronary anatomy) by two-dimensional echocardiography. Cardiac catheterization is rarely necessary or indicated.

Tetralogy of Fallot with pulmonary atresia

TOF with pulmonary atresia involves the features of TOF and infundibular and pulmonary valvular atresia in conjunction with varying degrees of pulmonary arterial atresia. Four groups are said to exist. Group 1 patients have isolated infundibular and pulmonary valve atresia with a main pulmonary artery (PA) and distal PAs of near normal size and architecture. In some of these patients, the main PA may extend to the atretic

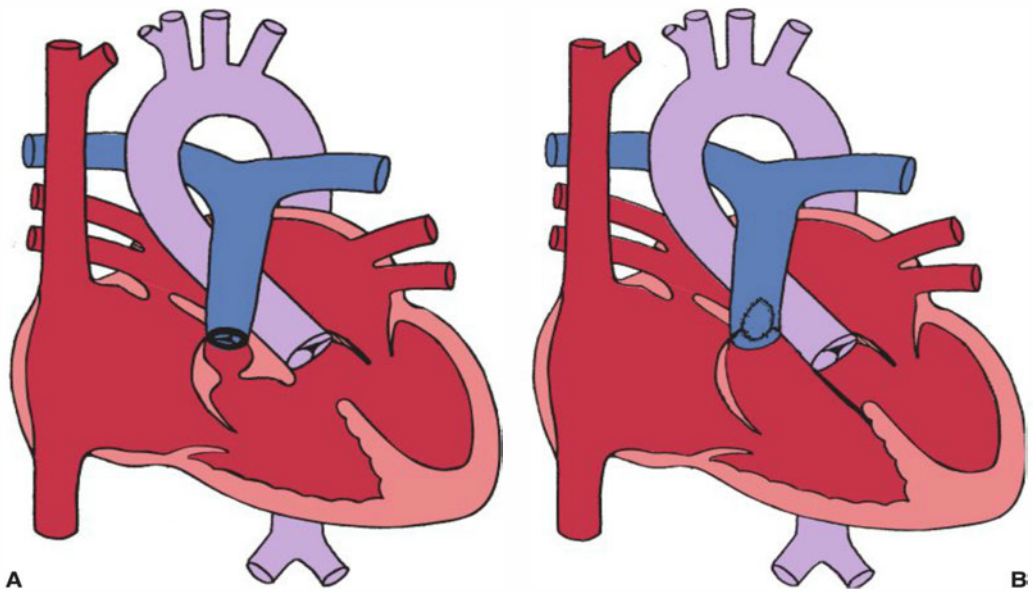

Figure 38.1 **A.** Uncorrected TOF/PS demonstrating malalignment VSD with aortic override, valvar and subvalvar (dynamic) PS. There is a left aortic arch. **B.** Definitively repaired tetralogy of Fallot with pulmonary stenosis (TOF/PS) with ventricular septal defect (VSD) closure creating left ventricle (LV) to aortic continuity, resection of subvalvar muscle bundles and deviated conal septum, and creation of a transannular patch (with pulmonary valvectomy) creating pulmonary insufficiency. A small atrial level communication has been left.

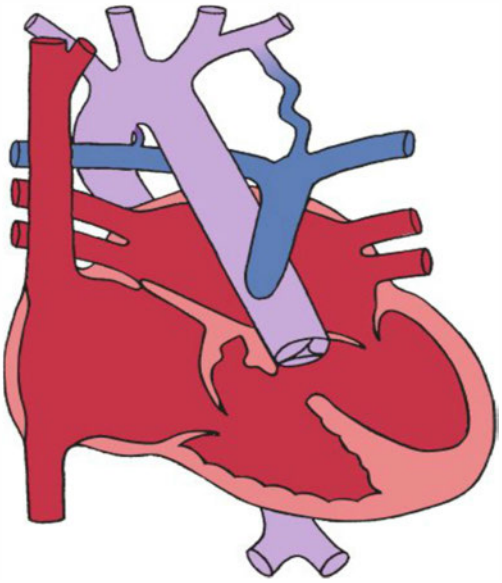

Figure 38.2 Illustration of tetralogy of Fallot with pulmonary atresia group 1 with short segment pulmonary artery, good-sized PAs in continuity supplied by a right-sided patent ductus arteriosus (PDA), and one major aortopulmonary collateral artery (MAPCA) from the left subclavian artery. There is a right aortic arch with mirror image arch vessel branching.

infundibulum. In others, there is short segment atresia of the main PA (Fig. 38.2). Patients in this group have pulmonary blood flow supplied from a patent ductus arteriosus (PDA). Group 2 patients have absence of the main PA, but the PAs are in continuity and supplied by a PDA. Group 3 patients have severely hypoplastic native PAs; the left and right PA may not be in continuity. There are major aortopulmonary collateral arteries (vessels from the aorta to the PA) known as *MAPCAs*. A PDA may be present as well. Some segments of lung may be supplied only by blood from MAPCAs, some only by the native PAs, and others by both sources (Fig. 38.3). Group 4 patients have no native PAs and all pulmonary blood flow is derived entirely from MAPCAs.

The anatomy of MAPCAs in TOF with pulmonary atresia can almost never be clearly delineated by two-dimensional echocardiography alone. Cardiac catheterization and/or magnetic resonance imaging/magnetic resonance angiography are necessary to delineate collateral anatomy and to determine $Q_P : Q_S$.

DiNardo JA. Anesthesia for congenital heart disease. In: DiNardo JA, Zvara DA, eds. *Anesthesia for Cardiac Surgery*. 3rd ed. Oxford: Blackwell Publishing; 2008:167–251.

Jonas RA, ed. Tetralogy of Fallot with pulmonary atresia. In: *Comprehensive Surgical Management of Congenital Heart Disease*. London: Arnold; 2004:440–456.

A.2. What is the pathophysiology of TOF with pulmonary stenosis (TOF/PS)?

TOF/PS is a complex shunt in which a communication (VSD) and a partial obstruction to RV outflow (RV infundibular and valvular stenosis) are present. In

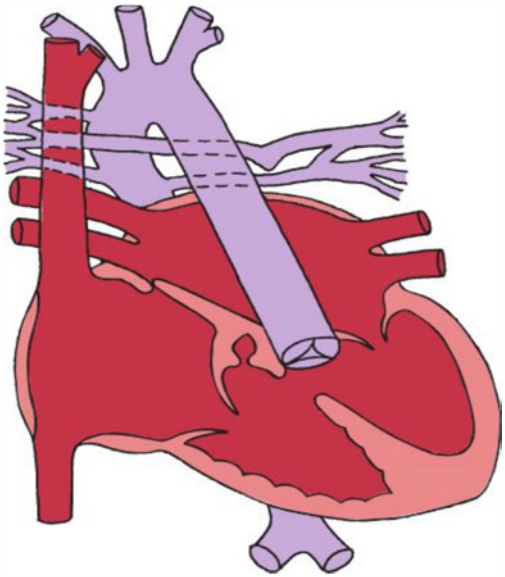

Figure 38.3 Illustration of tetralogy of Fallot with pulmonary atresia group 3 with no main PA, small branch PAs in continuity supplied by major aortopulmonary collateral arteries (MAPCAs). Some lung segments are supplied by the native PAs while others are supplied directly by MAPCAs. There is a right aortic arch with mirror image arch vessel branching.

complex shunts, the resistance to outflow is a combination of the resistance from the obstructive lesions and the vascular resistance. If the resistance from the RV obstructive lesions is high, changes in PVR will have little effect on shunt magnitude and direction. In most patients with TOF/PS, there is a fixed and a dynamic component to RV outflow obstruction. The fixed component is produced by the valvular stenosis. The dynamic component is produced by variations in the caliber of the RV infundibulum. The pathophysiology present in TOF/PS is physiologic right-to-left (R-L) shunting induced by the presence of a VSD and RVOT obstruction. In addition, because the aorta overrides the VSD and the RV, desaturated systemic venous blood tends to stream out the aorta even in the presence of mild RVOT obstruction.

The Sao_2 is determined by the relative volumes and saturations of recirculated systemic venous blood and effective systemic blood flows that have mixed and reached the aorta. This is summarized in the following equation:

$$\text{Aortic } Sao_2 = \frac{\begin{array}{c}([\text{pulmonary venous } O_2 \text{ saturation}]\,[\text{effective systemic blood flow}] \\ +\,[\text{systemic venous } O_2 \text{ saturation}]\,[\text{recirculated systemic venous blood flow}])\end{array}}{(\text{total sytemic blood flow})}$$

This is demonstrated in Figure 38.4 where the $Sao_2 = [(98)(0.5) + (65)(0.5)]/1 = 81$.

A.3. What is shunting and how is Q_P: Q_S calculated?

Shunting is the process whereby venous return into one circulatory system is recirculated through the arterial outflow of the same circulatory system. Flow of blood from the systemic venous atrium (right atrium) to the aorta produces recirculation of

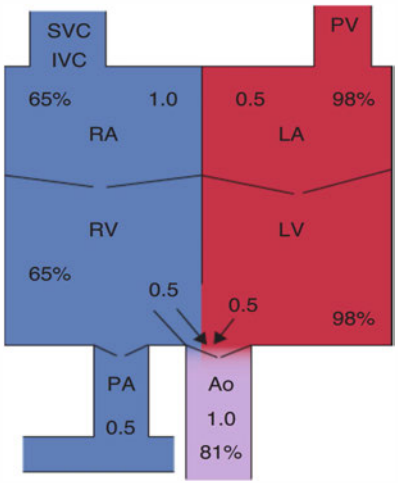

Figure 38.4 Chamber oxygen saturations and relative flows for a patient with uncorrected tetralogy of Fallot with pulmonary stenosis (TOF/PS). Arterial, oxygen saturation (Sao_2) and Q_P : Q_S are illustrated. Ao, aorta; IVC, inferior vena cava; LA, left atrium; LV, left ventricle; PA, pulmonary artery; PV, pulmonary vein; RA, right atrium; RV, right ventricle; SVC, superior vena cava.

systemic venous blood. Flow of blood from the pulmonary venous atrium (left atrium) to the PA produces recirculation of pulmonary venous blood. Recirculation of blood produces a physiologic shunt. Recirculation of pulmonary venous blood produces a physiologic left-to-right (L-R), whereas recirculation of systemic venous blood produces a physiologic R-L shunt. A physiologic R-L or L-R shunt commonly is the result of an anatomic R-L or L-R shunt. In an anatomic shunt, blood moves from one circulatory system to the other through a communication (orifice) at the level of the cardiac chambers or great vessels. Physiologic shunts can exist in the absence of an anatomic shunt; transposition physiology is the best example.

Effective blood flow is the quantity of venous blood from one circulatory system reaching the arterial system of the other circulatory system. Effective pulmonary blood flow is the volume of systemic venous blood reaching the pulmonary circulation, whereas effective systemic blood flow is the volume of pulmonary venous blood reaching the systemic circulation. Effective pulmonary blood flow and effective systemic blood flows are the flows necessary to maintain life. Effective pulmonary blood flow and effective systemic blood flow are always equal, no matter how complex the lesions. Effective blood flow usually is the result of a normal pathway through the heart, but it may occur as the result of an anatomic R-L or L-R shunt.

Total pulmonary blood flow (Q_P) is the sum of effective pulmonary blood flow and recirculated pulmonary blood flow. Total systemic blood flow (Q_S) is the sum of effective systemic blood flow and recirculated systemic blood flow. Total pulmonary blood flow and total systemic blood flow do not have to be equal. Because Q_S (systemic cardiac output) tends to remain constant to supply end organs, a physiologic L-R shunt (pulmonary recirculation) causes volume overload while a physiologic R-L shunt (systemic recirculation) allows Q_S to be maintained at the expense of Sao_2.

Calculation of $Q_P : Q_S$ (the ratio of total pulmonary blood flow to systemic blood flow) is greatly simplified when the determination is made using low inspired concentrations of oxygen. This allows the contribution of oxygen carried in solution ($Po_2 \times 0.003$) to be ignored. Failure to account for this component when determination of $Q_P : Q_S$ is made using a fraction of inspired oxygen (FIO_2) of 1.0 will introduce substantial (100%) error. If the FIO_2 is low, the determination of $Q_P : Q_S$ can be simplified to the following equation using just oxygen saturations:

$$(S_AO_2 - S_{SVC}O_2)/(S_{PV}O_2 - S_{PA}O_2)$$

where A = arterial, SVC = superior vena cava, PV = pulmonary vein that can be assumed to be 98% in the absence of significant pulmonary disease, and PA = pulmonary artery.

DiNardo JA. Anesthesia for congenital heart surgery. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart Disease*. London: Arnold; 2004:45–65.

A.4. What is the pathophysiology of TOF with pulmonary atresia?

The pathophysiology of TOF with pulmonary atresia is single ventricle physiology. Single ventricle physiology describes the situation wherein complete mixing of pulmonary venous and systemic venous blood occurs at the atrial or ventricular level and the ventricle(s) then distributes output to both the systemic and pulmonary beds. As a result of this physiology the following are observed:

- Ventricular output is the sum of pulmonary blood flow (Q_P) and systemic blood flow (Q_S)
- Distribution of systemic and pulmonary blood flow is dependent on the relative resistances to flow (both intracardiac and extracardiac) into the two parallel circuits
- Oxygen saturations are the same in the aorta and the PA

This physiology can exist in patients with one well-developed ventricle and one hypoplastic ventricle as well as in patients with two well-formed ventricles. In the case of a single anatomic ventricle, there is always obstruction to either pulmonary or systemic blood flow as the result of complete or near complete obstruction to inflow and/or outflow from the hypoplastic ventricle. In this circumstance, there must be a source of both systemic and pulmonary blood flow to ensure postnatal survival. In some instances of a single anatomic ventricle, a direct connection between the aorta and the PA through a PDA is the sole source of systemic blood flow (hypoplastic left heart syndrome) or of pulmonary blood flow (PA with intact ventricular septum). This is known as *ductal dependent circulation*. In other instances of a single anatomic ventricle, intracardiac pathways provide both systemic and pulmonary blood flow without the necessity of a PDA. This is the case in tricuspid atresia with normally related great vessels, a nonrestrictive VSD and minimal or absent PS.

In certain circumstances, single ventricle physiology can exist in the presence of two well-formed anatomic ventricles. This is generally the result of atresia or near atresia of outflow from one of the ventricles. Examples include the following:

- TOF with pulmonary atresia where pulmonary blood flow is supplied through a large PDA or MAPCAs
- Truncus arteriosus
- Severe neonatal aortic stenosis and interrupted aortic arch; in both lesions a substantial portion of systemic blood flow is supplied through a PDA
- Heterotaxy syndrome

DiNardo JA. Anesthesia for congenital heart surgery. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart Disease.* London: Arnold; 2004:45–65.

A.5. How is arterial O_2 saturation determined in single ventricle physiology?

With single ventricle physiology, the arterial oxygen saturation (Sao_2) will be determined by the relative volumes and saturations of pulmonary venous and systemic venous blood flows that have mixed and reached the aorta. This is summarized in the following equation:

$$\text{Aortic } O_2 \text{ saturation} = \frac{\begin{array}{c}([\text{systemic venous saturation}][\text{total systemic venous blood flow}] \\ +\ [\text{pulmonary venous saturation}][\text{total pulmonary venous blood flow}])\end{array}}{(\text{total systemic blood flow} + \text{total pulmonary venous blood flow})}.$$

The primary goal in the management of patients with single ventricle physiology is optimization of systemic oxygen delivery and perfusion pressure. This is necessary if end-organ (myocardial, renal, hepatic, splanchnic) dysfunction and failure are to be prevented. This goal is achieved by balancing the systemic and pulmonary circulations. The term *balanced circulation* is used because both laboratory and clinical evaluations have demonstrated that maximal systemic oxygen delivery (the product of systemic oxygen content and systemic blood flow) is achieved for single ventricle lesions when $Q_P : Q_S$ is at or just below 1:1. Increases in $Q_P : Q_S$ in excess of 1:1 are associated with a progressive decrease in systemic oxygen delivery because the subsequent increase in systemic oxygen content is more than offset by the progressive decrease in systemic blood flow and by diastolic hypotension due to run-off into the pulmonary circulation. Decreases in $Q_P : Q_S$ just below 1:1 are associated with a precipitous decrease in systemic oxygen delivery because the subsequent increase in systemic blood flow is more than offset by the dramatic decrease in systemic oxygen content.

DiNardo JA. Anesthesia for congenital heart surgery. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart Disease.* London: Arnold, 2004:45–65.

A.6. What is a "pink Tet"?

The term *pink Tet* refers to any noncyanotic patient with TOF/PS or TOF with pulmonary atresia. In these patients, $Q_P : Q_S$ is sufficiently high ($Q_P : Q_S$ generally greater than 0.8:1 in the presence of a normal mixed venous saturation and pulmonary vein saturation) to maintain a deoxyhemoglobin concentration less than 5 g per dL (Sao_2 generally >80%). The designation of "pink Tet" would apply to TOF/PS patients with minimal valvular and subvalvular PS and to all patients with TOF with pulmonary atresia where pulmonary blood flow is supplied from a large PDA and/or MAPCAs.

DiNardo JA. Anesthesia for congenital heart disease. In: DiNardo JA, Zvara DA, eds. *Anesthesia for Cardiac Surgery.* 3rd ed. Oxford: Blackwell Publishing; 2008:167–251.

A.7. What are hypercyanotic spells? How are they treated?

The occurrence of hypoxic spells in TOF patients may be life threatening and should be anticipated in every patient with TOF/ PS and any infundibular obstruction, even those who are not normally cyanotic. The peak frequency of spells is between 2 and 3 months of age; spells occur more frequently in severely cyanotic patients. The onset of spells usually prompts urgent surgical intervention, so it is not unusual

for the anesthesiologist to care for an infant who is at great risk for spells during the preoperative period. The etiology of spells is not completely understood, but infundibular spasm or constriction plays a role. Crying, defecation, feeding, fever, and awakening all can be precipitating events. Paroxysmal hyperpnea is the initial finding. There is an increase in rate and depth of respiration, leading to increasing cyanosis and potential syncope, convulsions, or death. During a spell, the infant will appear pale and limp secondary to poor cardiac output. Hyperpnea has several deleterious effects in maintaining and worsening a hypoxic spell. Hyperpnea increases oxygen consumption through the increased work of breathing. Hypoxia induces a decrease in systemic vascular resistance (SVR), which further increases the R-L shunt. Hyperpnea also lowers intrathoracic pressure and leads to an increase in systemic venous return. In the face of infundibular obstruction, this results in an increased RV pressure and an increase in the R-L shunt. Treatment of a "Tet spell" includes the following:

- Administration of 100% oxygen
- Compression of the femoral arteries or placing the patient in a knee-chest position transiently increases SVR and reduces the R-L shunt.
- Administration of morphine sulfate (0.05 to 0.1 mg/kg), which sedates the patient and may have a depressant effect on respiratory drive and hyperpnea
- Administration of 15 to 30 mL per kg of a crystalloid solution. Enhancing preload will increase heart size, which may increase the diameter of the RVOT.
- Administration of sodium bicarbonate to treat the severe metabolic acidosis that can be seen during a spell. Correction of the metabolic acidosis will help normalize SVR and reduce hyperpnea. Bicarbonate administration (1 to 2 mEq/kg) in the absence of a blood gas determination is warranted during a spell.
- Phenylephrine (dose 5 to 10 μg/kg IV or 2 to 5 μg/kg/minute as an infusion) can be used to increase SVR and reduce R-L shunting. In the presence of severe RV outflow obstruction, phenylephrine-induced increases of PVR will have little or no effect in increasing RV outflow resistance. It is important to point out that treatment with α-adrenergic agents to increase SVR does nothing to treat the underlying cause of the spell, although the decrease in unstressed venous volume induced by these agents may augment preload.
- β-Adrenergic agonists are absolutely contraindicated. By increasing contractility, they will cause further narrowing of the stenotic infundibulum.
- Administration of propranolol (0.1 mg/kg) or esmolol (0.5 mg/kg followed by an infusion of 50 to 300 μg/kg/minute) may reduce infundibular spasm by depressing contractility. In addition, slowing of heart rate may allow for improved diastolic filling (increased preload), increased heart size, and an increase in the diameter of the RVOT.
- Manual compression of the abdominal aorta will increase SVR; this maneuver is particularly effective for the anesthetized patient. After the chest is open, the surgeon can manually compress the ascending aorta to increase impedance to ejection through the LV. This can be effective in terminating a cyanotic episode.
- Extracorporeal membrane oxygenation resuscitation is another alternative in refractory episodes when immediate operative intervention is not possible.

DiNardo JA. Anesthesia for congenital heart disease. In: DiNardo JA, Zvara DA, eds. *Anesthesia for Cardiac Surgery*. 3rd ed. Oxford: Blackwell Publishing; 2008:167–251.

A.8. What palliative surgical procedures are available for treating this patient with TOF/PS?

Palliative shunt procedures to increase pulmonary blood flow can be used for patients with TOF/PS in whom complicated surgical anatomy precludes definitive repair at

the time of presentation. In addition, some institutions delay elective complete repair until 12 to 18 months of age with placement of a palliative shunt if cyanosis occurs before that time interval. The palliative shunt procedures involve creation of a systemic-to-pulmonary arterial shunt analogous to a PDA. Ideally, these surgical shunts should be mildly restrictive simple shunts. In the presence of a proximal obstruction to pulmonary blood flow, these shunts produce an L-R shunt and an increase in pulmonary blood flow. The volume load imposed on the LV by these shunts parallels the increases in pulmonary flow that they produce. There will be progressive hypertrophy of the body and infundibulum of the RV during the interval from shunt placement to definitive repair as RVOT obstruction will not be relieved. The shunts can be summarized as follows:

Waterston shunt—this shunt results from creation of a side-to-side anastomosis between the ascending aorta and the right PA. This procedure is performed through a right thoracotomy without CPB.

Potts shunt—this shunt results from creation of a side-to-side anastomosis between the descending aorta and the left PA. This procedure is performed through a left thoracotomy without CPB.

Waterston and Potts shunts are of historic interest only. It is difficult to size the orifice of this shunt correctly. Too small an orifice will limit pulmonary blood flow, whereas too large an orifice will create pulmonary overperfusion and congestion and predispose to development of unilateral pulmonary vascular obstructive disease. These shunts may produce distortion of the PA, making subsequent definitive repair difficult. In addition, they are difficult to take down at the time of the definitive procedure.

Central shunt—placing a synthetic tube graft between the ascending aorta and the main or branch PA creates this shunt. This shunt can be performed with or without CPB through a thoracotomy or median sternotomy. It often is used when prior shunt procedures have failed.

Blalock-Taussig shunt (BTS)—as originally described this involved creation of an end-to-side anastomosis of the right or left subclavian artery to the ipsilateral branch PA. Currently, a modification of this procedure known as the *modified Blalock-Taussig shunt* (*MBTS*) is used. It involves interposing a length of Gore-Tex tube graft (3.5 to 4.0 mm in infants) between the subclavian or innominate artery and the branch PA. These shunts usually are performed on the side opposite the aortic arch through a thoracotomy without CPB (Fig. 38.5).

DiNardo JA. Anesthesia for congenital heart disease. In: DiNardo JA, Zvara DA, eds. *Anesthesia for Cardiac Surgery*. 3rd ed. Oxford: Blackwell Publishing; 2008:167–251.

A.9. What definite surgical procedures are available for treating this patient with TOF/PS?

Currently, most patients with TOF/PS have an elective full correction between the ages of 2 and 10 months of age. In some centers, surgery is delayed as long as possible within this time interval, with the precise timing of repair dictated by the onset of cyanotic episodes. Definitive repair for TOF/PS is being accomplished in neonates in some centers if favorable anatomy is present. Surgery is aimed at relieving the outflow obstruction by resection of hypertrophied, obstructing muscle bundles and augmentation and enlargement of the outflow tract with a pericardial patch. Unless the pulmonic annulus is near normal size and the pulmonary valve is only mildly stenotic, enlargement of the outflow tract involves extension of the patch across the pulmonary valve annulus and into the main PA. Because a transannular patch creates pulmonic insufficiency, it is avoided when possible. If stenosis of the PA extends to the bifurcation, the pericardial patch can be extended beyond the bifurcation of the pulmonary arteries.

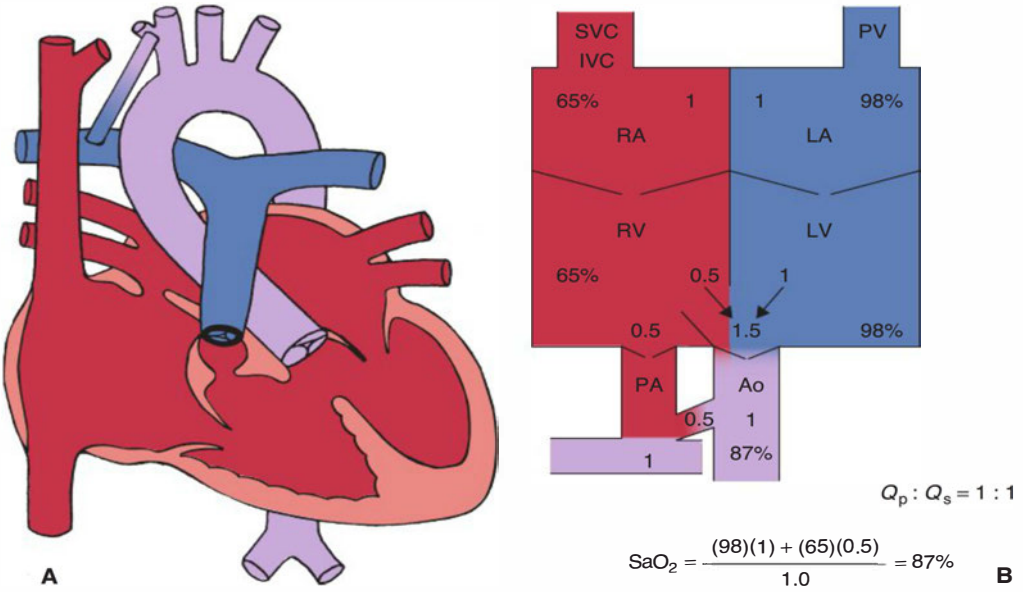

Figure 38.5 **A.** Palliative modified Blalock-Taussig shunt (MBTS) for tetralogy of Fallot with pulmonary stenosis (TOF/PS). Shunt is seen to connect the innominate artery to the right pulmonary artery (PA). This patient has a left aortic arch. **B.** Chamber oxygen saturations and relative flows for a patient with MBTS and TOF/PS. Arterial oxygen saturation (SaO_2) and $Q_P : Q_S$ are illustrated. Ao, aorta; IVC, inferior vena cava; LA, left atrium; LV, left ventricle; PV, pulmonary vein; RA, right atrium; RV, right ventricle; SVC, superior vena cava.

Finally, the VSD is closed. In neonates, this is usually done through the right ventriculotomy created for resection of RVOT obstruction and placement of the transannular patch. In infants and older children, the VSD can be closed through a transtricuspid valve approach.

An important surgical consideration for patients with TOF/PS is the occurrence of coronary artery abnormalities. Approximately 8% of patients have either the left main coronary artery or the left anterior descending artery as a branch of the right coronary artery. In these cases, a right ventriculotomy to enlarge the RVOT will endanger the left coronary artery. In such cases, an extracardiac conduit (RV to main PA) may be necessary to bypass the outflow tract obstruction and avoid injury to the coronary artery.

DiNardo JA. Anesthesia for congenital heart disease. In: DiNardo JA, Zvara DA, eds. *Anesthesia for Cardiac Surgery*. 3rd ed. Oxford: Blackwell Publishing; 2008:167–251.

Jonas RA, ed. Tetralogy of Fallot with pulmonary stenosis. In: *Comprehensive Surgical Management of Congenital Heart Disease*. London: Arnold; 2004:279–300.

A.10. What palliative and definite surgical procedures are available for treating a patient with TOF with pulmonary atresia?

Surgery in group 1 and 2 TOF with pulmonary atresia patients is aimed at establishing a reliable source of pulmonary blood flow in the neonatal period, as these patients

are dependent on prostaglandin E_1 ($PGE1_1$) to maintain a PDA and pulmonary blood flow. These patients may undergo a palliative shunt procedure or a definite procedure. The definite procedure would be creation of continuity between the RV and the main PA through placement of an RV to PA conduit with VSD closure generally performed through the ventriculotomy used for the proximal end of the conduit. Patients in groups 3 and 4 present difficult management problems. As a rule, these patients present with univentricular physiology with a tendency for pulmonary blood flow to become excessive ($Q_P : Q_S > 2$ to 3:1) as the PVR drops following birth. In group 3 patients, neonatal repair with placement of an RV to PA conduit is undertaken to place the PAs in continuity with the RV in an effort to promote native PA growth. In this circumstance, the VSD is left open as a source of R-L shunting and delivery of desaturated blood to the systemic circulation because it would be impossible for the RV to deliver an adequate cardiac output to the left atrium across the hypoplastic pulmonary vascular bed. These infants then undergo multiple cardiac catheterization procedures in order to (1) dilate and stent the hypoplastic native PAs, and (2) to coil embolize MAPCAs, which provide pulmonary blood flow that is competitive with blood flow supplied by native PAs. MAPCAs that provide pulmonary blood flow to segments of lung not supplied by native PAs must be unifocalized to the proximal pulmonary circulation.

Unifocalization may have to be performed and involves removal of the collateral vessel from the aorta with subsequent reanastomosis to the RV to PA conduit or a proximal PA branch. Although the traditional approach has been through a thoracotomy, more recently, most groups have favored a central approach working through a median sternotomy. It is only when 80% to 90% of the pulmonary vascular bed is direct continuity with the RV that closure or fenestrated closure of the VSD can be considered. Usually, this will mean that at least 10 to 12 bronchopulmonary segments are now in direct continuity with the RV.

In group 4 patients, it may be necessary to unifocalize several large collaterals to the distal end of conduit from the RV as the initial intervention. Alternatively, several large collaterals could be unifocalized to an MBTS or central shunt. These procedures serve to promote pulmonary vascular growth, prevent the development of pulmonary vascular obstructive disease, and control the $Q_P : Q_S$.

Jonas RA, ed. Tetralogy of Fallot with pulmonary atresia. In: *Comprehensive Surgical Management of Congenital Heart Disease*. London: Arnold, 2004:440–456.

B. Preoperative Evaluation and Preparation

B.1. What preoperative history and physical examination information do you want?

Clinical history should include medications, allergies, past hospitalizations and operations (including prior anesthetic experiences), and a thorough review of systems. Performance of age-appropriate activities will aid in the evaluation of cardiac function and reserve. The neonate and infant in cardiac failure will manifest symptoms of low cardiac reserve during feeding, which is a strenuous activity, even for a normal newborn. A parent might report that sweating, tiring, dyspnea, and circumoral cyanosis occur during feeding. The observation by a parent that the patient cannot keep the same pace as siblings often is a reliable clinical sign that cyanosis or congestive heart failure is worsening.

Interpretation of vital signs must be age-specific. Growth curves also are useful. Congestive heart failure will inhibit, sequentially, age-appropriate gains

in weight, height, and head circumference. It is not unusual for patients with severe congestive heart failure to weigh less at 3 or 4 months of age than at birth. Interestingly, cyanotic children often do not manifest this failure to thrive. Physical examination will reveal cyanosis, clubbing, or signs of congestive heart failure similar to those seen in adults, such as hepatomegaly, ascites, edema, or tachypnea. Rales may not be heard in infants and children with congestive heart failure, and the degree of heart failure may be determined more reliably by some of the signs and symptoms outlined in the preceding text. The degree of cyanosis is related to the percentage of desaturated hemoglobin. A markedly hypoxemic child with baseline arterial saturations in the 70% range may be anemic and clinically appear less cyanotic than another child with similar arterial saturation and a more appropriate hematocrit of 65%.

Physical examination should include an evaluation of the limitations to vascular access and monitoring sites imposed by previous surgery. A child who has undergone a palliative shunt procedure may have a diminished pulse or unobtainable blood pressure in the arm in which the subclavian artery has been incorporated into the shunt. This obviously has implications for arterial catheter placement, sphygmomanometric blood pressure monitoring, and use of pulse oximetry during surgery. Finally, the child who has undergone multiple palliative procedures may have poor venous access, which may influence the mode of induction.

It often is difficult to differentiate clearly between signs and symptoms of congestive heart failure and a mild upper respiratory tract infection. Because increased pulmonary blood flow seems to predispose multiple respiratory tract infections, the physical examination may show mild tachypnea, wheezing, or upper airway congestion and, in the absence of abnormal laboratory findings or fever, may be impossible to distinguish from congestive heart failure. The decision to proceed to surgery may be necessary even when the differentiation between worsening congestive heart failure and a respiratory tract infection cannot be made with certainty.

DiNardo JA. Anesthesia for congenital heart disease. In: DiNardo JA, Zvara DA, eds. *Anesthesia for Cardiac Surgery*. 3rd ed. Oxford: Blackwell Publishing; 2008:167–251.

B.2. Which other abnormalities need to be considered in this patient?

Because approximately 8% of children with congenital heart disease have other congenital abnormalities, it is prudent to consider and define these defects. For example, patients with TOF/PS and TOF with pulmonary atresia have a higher incidence of 22q11.2 deletion, a defect associated with DiGeorge syndrome, velocardiofacial syndrome, and conotruncal anomaly face syndromes leading to hypocalcemia, immunodeficiency, facial dysmorphia, palate anomalies, velopharyngeal dysfunction, renal anomalies, and speech and feeding disorders as well as neurocognitive, behavioral, and psychiatric disorders. Tracheal stenosis and bronchomalacia may be a serious problem for TOF with pulmonary atresia patients who have undergone tracheoesophageal fistula repair. Needless to say, many of these defects can seriously complicate airway management.

DiNardo JA. Anesthesia for congenital heart disease. In: DiNardo JA, Zvara DA, eds. *Anesthesia for Cardiac Surgery*. 3rd ed. Oxford: Blackwell Publishing; 2008:167–251.

Kobrynski LJ, Sullivan KE. Velocardiofacial syndrome, DiGeorge syndrome: the chromosome 22q11.2 deletion syndromes. *Lancet*. 2007; 370:1443–52.

B.3. In general, what nothing by mouth (NPO) guidelines will you follow and what premedication will you give to a child with congenital heart disease?

Generally speaking, the rule of 2, 4, 6, 8 can be used as the NPO interval for neonates, infants, and children with congenital heart disease:

- 2 hours for clear liquids
- 4 hours for breast milk
- 6 hours for formula
- 8 hours for solid food

Premedication before induction can be used to facilitate a number of objectives. In older children, it can be used to alleviate anxiety before an IV or inhalation induction. In younger children, premedication eases separation of the child from the parents. In infants, judicious premedication alone or in combination with inhaled nitrous oxide can greatly simplify placement of an IV catheter in an otherwise struggling infant. Midazolam 1.0 mg per kg orally in infants and younger children who have not had prior cardiac surgery is useful. In children older than 1 year who have undergone prior operative procedures, oral ketamine 7 to 10 mg per kg in combination with midazolam 1.0 mg per kg works well. These children are remarkably tolerant to midazolam as the result of either heightened anxiety or previous intraoperative and postoperative exposure to benzodiazepines. In circumstances where premedication is deemed important and the child will not take oral medication, the intramuscular route can be used. Ketamine 2 to 3 mg per kg and glycopyrrolate (10 μg/kg) alone or in combination with midazolam 0.1 mg per kg works well.

DiNardo JA. Anesthesia for congenital heart surgery. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart Disease*. London: Arnold; 2004:45–65.

Ferrari LR, Rooney FM, Rockoff MA. Preoperative fasting practices in pediatrics. *Anesthesiology*. 1999;90:978–980.

C. Intraoperative Management

C.1. How will you induce anesthesia in this patient if intravenous (IV) access cannot be obtained?

An alternative to IV induction in infants and neonates with difficult peripheral IV access is intramuscular induction with ketamine (3 to 5 mg/kg), succinylcholine (5 mg/kg), and glycopyrrolate (10 μg/kg). Glycopyrrolate is recommended to reduce the airway secretions associated with ketamine administration and to prevent the bradycardia, which may accompany succinylcholine administration. This technique provides prompt induction and immediate control of the airway with tracheal intubation and is useful in circumstances where it is anticipated that initial IV access will have to be obtained through the external jugular vein, femoral vein, or internal jugular vein. This technique is hampered by the fact that the short duration of action of succinylcholine limits the period of patient immobility. An alternative technique combines intramuscular ketamine (4 to 5 mg/kg), glycopyrrolate (10 μg/kg), and rocuronium (1.0 mg/kg). This technique is hampered by the longer time interval until attainment of adequate intubating conditions and the longer duration of action of rocuronium as compared to succinylcholine.

DiNardo JA. Anesthesia for congenital heart surgery. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart Disease*. London: Arnold; 2004:45–65.

C.2. Why would end-tidal carbon dioxide ($ETco_2$) monitoring be of particular use in a patient with TOF/PS?

$ETCO_2$ monitoring is routinely employed in patients with congenital heart disease, with the caveat that the difference between $Paco_2$ and $ETco_2$ will vary as physiologic dead space varies and that, in some circumstances, the difference may be large (>10 to 15 mm Hg). Any acute reduction in pulmonary blood flow (decreased cardiac output, pulmonary embolus, increased intracardiac R-L shunting) will increase this gradient. In a patient with TOF/PS, a gradual reduction in $ETco_2$ will often precede a decrease in Sao_2 as the first manifestation of the increased R-L intracardiac shunting associated with a "Tet spell."

DiNardo JA. Anesthesia for congenital heart surgery. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart Disease.* London: Arnold; 2004:45–65.

C.3. What is near-infrared spectroscopy (NIRS) and what does it measure?

NIRS is an evolving technology that holds promise as a real-time, online monitor of cerebral tissue oxygenation. This technology is based on the physical principle that light of an appropriate wavelength passing through a solution of a colored compound (chromophore) will be absorbed by the compound. As a result of this absorption, the intensity of the light emerging from the solution will be lower than the intensity of the light projected into the solution. This principle through application of the Beer-Lambert equation "$\log [I_O/I] = c\ \alpha\ d$" allows quantification of the concentration (c) of a chromophore if the emergent light intensity (I) is measured and the following are known:

- Extinction coefficient (α), a constant that describes the absorption characteristics of a particular chromophore at a given wavelength of light
- Thickness of the solution (d)
- Incident light intensity (I_O)

NIRS technology is particularly suited to use in neonates and infants because the thin skull and small head allow light to be transmitted through one side of the head and detected on the other side, a technique known as *transmission spectrometry*.

Cerebral oxygen saturation (Sco_2) as measured by all NIRS technology is the combined oxygen saturation of an uncertain mix of arterioles, capillaries, and venules. Traditional pulse oximetry differs in this respect from NIRS because it is capable of isolating and measuring the arteriole component by gating measurements to pulsatility. It has been previously assumed that Sco_2 represented contributions of cerebral arterial and venous blood in a ratio of 25:75, with the contribution of capillary blood felt to be negligible. More recent data suggest that in children, the average ratio is 15:85. The issue is further complicated by the fact that there is significant variability in the ratio (from 0:100 to 40:60) between patients.

DiNardo JA. Anesthesia for congenital heart surgery. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart Disease.* London: Arnold; 2004:45–65.

C.4. What are the important management issues during creation of a palliative shunt?

- When a thoracotomy approach is used, unilateral lung retraction will be required for surgical exposure. The resulting atelectasis may severely compromise oxygenation

and CO_2 removal. Intermittent reinflation of the lung may be necessary during the operative procedure. These reinflations should be coordinated with the surgeon. For all the shunts described, the main or branch PA will have to be partially occluded by a clamp to allow creation of the distal anastomosis. The resulting increase in physiologic dead space may compromise oxygenation and CO_2 removal and will increase the arterial $ETCO_2$ gradient.

- Efforts to increase pulmonary blood flow by reducing PVR with ventilatory interventions and by increasing L-R shunting should be initiated before PA occlusion.
- Partial occlusion of the aorta with a clamp will be necessary during creation of Waterston, Potts, and central shunts. The resulting increase in LV afterload may compromise systolic function.
- All of the palliative shunts impose a volume load on the LV. Inotropic support may be necessary to ensure systemic and shunt perfusion after shunt creation.
- Palliative shunts are mildly restrictive simple shunts. It is important to maintain SVR and reduce PVR to maintain pulmonary blood flow in patients with surgical shunts.
- Be prepared to treat an episode of hypercyanosis.

DiNardo JA. Anesthesia for congenital heart disease. In: DiNardo JA, Zvara DA, eds. *Anesthesia for Cardiac Surgery*. 3rd ed. Oxford: Blackwell Publishing; 2008:167–251.

C.5. What is the effect of inhalation anesthetics on airway reflexes, myocardial contractility, systemic vascular resistance (SVR), and pulmonary vascular resistance (PVR) in children?

Sevoflurane, isoflurane, and desflurane all induce dose-related myocardial depression and SVR reduction with mild depression of contractility noted at 1 and 1.5 minimal alveolar concentration (MAC). Halothane induces a greater degree of myocardial depression at 1 and 1.5 MAC than sevoflurane, isoflurane, or desflurane. At these concentrations, neither sevoflurane, isoflurane, nor halothane alters the ratio of PVR to SVR substantially enough to induce any change in $Q_P : Q_S$.

Isoflurane and, particularly, desflurane are not good choices for inhalational induction because their pungency is responsible for a high incidence of airway complications in children. Desflurane has hemodynamic effects similar to isoflurane and may be useful as an adjuvant to narcotic anesthesia or as a primary maintenance agent after the airway has been secured. Sevoflurane has cardiovascular effects similar to isoflurane and is a good agent for inhalational induction in children; the incidence of airway complications is similar to that of halothane. Perhaps more important is the fact that inhalational induction with sevoflurane causes less myocardial depression than halothane in children.

DiNardo JA. Anesthesia for congenital heart disease. In: DiNardo JA, Zvara DA, eds. *Anesthesia for Cardiac Surgery*. 3rd ed. Oxford: Blackwell Publishing; 2008:167–251.

Laird TH, Stayer SA, Rivenes SM, et al. Pulmonary-to-systemic blood flow ratio effects of sevoflurane, isoflurane, halothane, and fentanyl/midazolam with 100% oxygen in children with congenital heart disease. *Anesth Analg*. 2002;95:1200–1206.

C.6. What are the pre–cardiopulmonary bypass (CPB) anesthetic goals for a patient undergoing definitive surgical correction of TOF/PS?

- Maintain heart rate, contractility, and preload to maintain cardiac output. Euvolemia is important to prevent exacerbation of dynamic RVOT obstruction from hypovolemia and reflex increases in heart rate and contractility.

- Avoid increases in the PVR : SVR ratio. The less severe the RV outflow obstructive lesions, the more important this becomes. Increases in PVR relative to SVR, and decreases in SVR relative to PVR, will increase R-L shunting, reduce pulmonary blood flow, and produce or worsen cyanosis.
- Use ventilatory measures to reduce PVR.
- Maintain or increase SVR. This is particularly important when RV outflow obstruction is severe and changes in PVR will have little or no effect on shunt magnitude and direction.
- Aggressively treat episodes of hypercyanosis.
- Maintain contractility. Depression of contractility, particularly in the face of severe RV outflow obstruction, may produce RV afterload mismatch and drastically reduce pulmonary blood flow. The exception to this is a patient in whom the dynamic component of infundibular obstruction is active. Reducing contractility in these patients may reduce RV outflow obstruction through relaxation of the infundibulum.

DiNardo JA. Anesthesia for congenital heart disease. In: DiNardo JA, Zvara DA, eds. *Anesthesia for Cardiac Surgery*. 3rd ed. Oxford: Blackwell Publishing; 2008: 167–251.

C.7. What interventions will reliably reduce PVR?

Po_2. Both alveolar hypoxia and arterial hypoxemia induce pulmonary vasoconstriction. An arterial O_2 tension lower than 50 mm Hg increases PVR over a wide range of arterial pH; however, this effect is enhanced when pH is lower than 7.40. Conversely, high levels of inspired O_2 can reduce an elevated PVR.

Pco_2. Hypercarbia increases PVR, independent of changes in arterial pH. Hypocarbia, on the other hand, reduces PVR only through production of an alkalosis. In fact, reliable reductions in PVR and increases in pulmonary blood flow and Po_2 are seen in children with R-L shunts when hyperventilation to a Pco_2 near 30 mm Hg and a pH near 7.50 is instituted. Similarly, postbypass hyperventilation to a Pco_2 of 30 to 35 mm Hg and a pH of 7.50 to 7.56 in patients with preoperative pulmonary hypertension results in a reduction in PVR when compared with ventilation that produces normocarbia or hypercarbia.

pH. Both respiratory and metabolic alkalosis reduce PVR, whereas both respiratory and metabolic acidosis increase PVR.

Variation in lung volumes. At small lung volumes, atelectasis results in compression of extra-alveolar vessels, whereas at high lung volumes, hyperinflation of alveoli results in compression of intra-alveolar vessels. Therefore, PVR is normally lowest at lung volumes at or near the functional residual capacity. Positive end-expiratory pressure (PEEP) may cause an increase in PVR by increasing alveolar pressure through hyperinflation. However, in situations in which PEEP works to recruit atelectatic alveoli and increase arterial Po_2, a decrease in PVR generally is seen.

Vasodilator agents. There is no IV drug that selectively acts as a pulmonary vasodilator. In general, IV drugs intended to induce pulmonary vasodilation (PGE_1, PGI_2, nitroglycerin, sodium nitroprusside, and tolazoline) induce systemic vasodilation as well. Inhaled nitric oxide, PGE_1, and PGI_2 are the only specific pulmonary vasodilators available.

DiNardo JA. Anesthesia for congenital heart disease. In: DiNardo JA, Zvara DA, eds. *Anesthesia for Cardiac Surgery*. 3rd ed. Oxford: Blackwell Publishing; 2008: 167–251.

C.8. How does heparin administration and activated coagulation time (ACT) monitoring differ in children as compared with adults?

Before use of cardiotomy suction, cannulation, and commencing bypass, it is essential that adequate anticoagulation be obtained. Unfractionated heparin is currently the anticoagulant used for CPB. It generally is acknowledged that an ACT in excess of 400 seconds is necessary to ensure adequate anticoagulation for the safe conduct of CPB.

While there is a large heparin anticoagulation monitoring literature in adults, there is a very small literature in children. The ACT, commonly used to assess CPB anticoagulation, is also prolonged by hypothermia, hemodilution, platelet dysfunction, and low coagulation factor levels. As a result, in children, the ACT will overestimate the antifactor IIa and Xa effects of heparin.

Most institutions use an age- or weight-based protocol to administer the initial pre-CPB dose of heparin such as patients less than 30 kg—200 IU per kg; or patients greater than 30 kg—300 IU per kg. The large circuit prime volume to blood volume ratio would be expected to decrease plasma heparin levels with initiation of CPB unless an appropriate quantity of heparin is added to the CPB prime. Most institutions add heparin to the CPB prime as follows: patients less than 30 kg—2.5 IU per mL of CPB prime; or patients greater than 30 kg—3.0 IU per mL of CPB prime.

Heparin should always be given into a central line through which venous return can be demonstrated easily or as is more common in infants/neonates directly into the heart (usually the right atrium) by the surgeon. This is necessary to ensure that the heparin dose has reached the central circulation. An ACT can be drawn within minutes of heparin administration as peak arterial ACT prolongation occurs within 30 seconds and peak venous ACT prolongation within 60 seconds.

DiNardo JA. Physiology and techniques of extracorporeal circulation in the pediatric patient. In: Lake CL, Booker, PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2005:228–252.

C.9. How is heparin reversed?

Protamine is a polyvalent cation derived from salmon sperm that is currently used to neutralize systemic heparinization. Protamine normally is given once stable hemodynamics are maintained after termination of CPB. It should not be administered until the likelihood that having to reinstitute CPB is small. After protamine neutralization of heparin begins, the cardiotomy suction should not be used and removal of the arterial and venous cannulas should proceed. This prevents contamination of the heparinized CPB circuit with protamine should prompt reinstitution of CPB be necessary and prevents thrombus formation on the cannulas.

There are several approaches to the neutralization of heparin with protamine, all with reportedly good clinical results. Some centers use 1.0 to 1.3 mg of protamine for each 100 units of heparin determined to exist at the termination of CPB. This ratio is based on the in vitro protamine-heparin neutralization ratio of 1.3:1.0. The amount of heparin present is determined by obtaining an ACT when CPB terminates and using reverse extrapolation of the patient's heparin dose response curve to correlate ACT and heparin dose. This method has been criticized because the ACT obtained at the termination of CPB is prolonged by factors other than heparin, such as CPB-induced platelet dysfunction and hemodilution. This may result in an overestimation of the heparin present at the termination of CPB and a larger than necessary protamine dose.

Some centers simply administer a fixed dose of protamine based on the patient's weight (3 to 4 mg/kg) regardless of the heparin dose administered, whereas others

administer 1.0 to 1.3 mg of protamine for each 100 units of heparin administered. Obviously, these methods do not rely on any post-CPB assessment of residual heparin effect (ACT) to determine the protamine dose. Nonetheless, these methods have been shown to result in adequate heparin reversal. In the case of the fixed dose regimen, heparin reversal is obtained at much lower protamine doses than predicted by the reverse extrapolation method.

The Hepcon automated heparin protamine titration method measures clotting times enhanced by addition of thromboplastin in several channels that contain varying quantities of protamine. The first channel to clot is the channel in which the protamine to heparin ratio is closest to neutralization. The absolute clotting time is not important; only the determination of the channel with the appropriate ratio. Therefore, the determination should be independent of nonheparin factors that prolong the ACT. In theory, this method should allow determination of the appropriate dose of protamine independent of the nonheparin parameters that prolong ACT.

DiNardo JA. Physiology and techniques of extracorporeal circulation in the pediatric patient. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2005:228–252.

C.10. What is the incidence of protamine reactions in children?

The incidence of protamine reactions in children following cardiac surgery is generally believed to be substantially lower than that in adults. A recent retrospective analysis of 1,249 children revealed the incidence of hypotension (at least 25% decrease in mean arterial pressure) following protamine administration to be 1.76% to 2.88%, depending on the stringency of criteria linking the episode to protamine administration. In this series, no episodes of pulmonary hypertension or RV dysfunction were noted. There is a report of pulmonary hypertension and cardiovascular collapse in 6-week-old infant following protamine administration. Clinical experience indicates that pulmonary hypertensive episodes in children following protamine administration are very rare.

DiNardo JA. Physiology and techniques of extracorporeal circulation in the pediatric patient. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2005:228–252.

C.11. What is the role of transesophageal echocardiography (TEE) in this patient?

It has been demonstrated that intraoperative TEE has a major impact on post-CPB decision making (such as return to CPB to repair residual lesions) in approximately 15% of cases when it is used nonselectively. In the subset of patients undergoing valve repair and outflow tract reconstruction, TEE provides the best immediate assessment of the adequacy of the operative procedure and, if necessary, directs its revision. While detection of retained intracardiac air is certainly facilitated by the use of intraoperative TEE, it remains to be determined what role the technology will play in improving cardiac de-airing algorithms particularly in neonates/infants.

The role of TEE in the detection of residual VSDs following repair of both simple and complex defects deserves some discussion. Residual defects less than 3 mm are detectable by TEE but generally do not require immediate reoperation because they are hemodynamically insignificant. The majority (75%) of these small defects are not present at the time of hospital discharge as determined by transthoracic echocardiography. Residual defects greater than 3 mm detected by TEE require immediate

reoperation only if they are associated with intraoperative hemodynamic (elevated left atrial pressure and/or pulmonary artery pressure in the presence of good ventricular function) and oximetric ($Q_P : Q_S$ >1.5 : 1 or right atrium to PA oxygen saturation step-up with fraction of inspired oxygen [F_{IO_2}] ≤0.50) evidence that they are significant.

DiNardo JA. Anesthesia for congenital heart surgery. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart disease*. London: Arnold; 2004:45–65.

Yang SG, Novello R, Nicolson S, et al. Evaluation of ventricular septal defect repair using intraoperative transesophageal echocardiography: frequency and significance of residual defects in infants and children. *Echocardiography*. 2000;17:681–684.

C.12. What effect would a residual ventricular septal defect (VSD) have in this patient following separation from CPB?

A residual VSD is likely to be very poorly tolerated in the patient with TOF/PS. The most likely manifestation is low cardiac output syndrome associated with elevated central venous pressure, left atrial pressure, and pulmonary artery pressure. RVOT obstruction will be completely or near completely eliminated postrepair. PVR is likely to be low and the pulmonary vasculature is likely to be very compliant. As a result there will be potential for a large L-R intracardiac shunt with a residual VSD. This will place a large volume load on the LV and RV. An acute volume load will not be well tolerated by the RV, which is likely to be concentrically hypertrophied and poorly compliant in response to the chronic pressure overload that existed preoperatively. The presence of pulmonary insufficiency will further exacerbate RV dysfunction by imposing an additional volume load.

DiNardo JA. Anesthesia for congenital heart disease. In: DiNardo JA, Zvara DA, eds. *Anesthesia for Cardiac Surgery*. 3rd ed. Oxford: Blackwell Publishing; 2008:167–251.

D. Postoperative Management

D.1. How should postoperative ventilation be managed in this patient following placement of a transannular patch for TOF/PS?

The inspiratory phase of mechanical positive pressure ventilation increases impedance to RV ejection by increasing RV afterload by elevating alveolar pressure and creating more West Zone I and II lung segments. As a result, the extent of this afterload elevation is directly related to the duration of inspiration (respiratory rate and I : E ratio) and to mean airway pressure. Increasing RV afterload will impede antegrade pulmonary blood flow and exacerbate the extent of pulmonary insufficiency induced by the transannular patch. RV afterload will also be increased by elevations in PVR.

As discussed in section C.7, ventilation and gas mixture should be adjusted to minimize PVR. This should be accomplished with a tidal volume of 10 to 15 mL per kg, 3 to 5 mm Hg of PEEP, and a respiratory rate and I : E ratio adjusted to minimize mean airway pressure.

DiNardo JA. Anesthesia for congenital heart disease. In: DiNardo JA, Zvara DA, eds. *Anesthesia for Cardiac Surgery*. 3rd ed. Oxford: Blackwell Publishing; 2008:167–251.

D.2. Following complete repair of TOF/PS in an infant, what arterial oxygen saturation (Sao_2) is acceptable?

Following complete repair of TOF/PS with no residual lesions and minimal intrapulmonary shunt, the Sao_2 should be 100%. In infants and small children, particularly those left with pulmonary insufficiency as the result of a transannular patch and those expected to have restrictive RV function as a result of a ventriculotomy and/or extensive RV hypertrophy, the surgeon may choose to leave a small (3 to 4 mm) atrial level communication or patent foramen ovale. This will allow intracardiac R-L shunting, with the ability to augment systemic cardiac output at the expense of systemic oxygen saturation in the setting of RV dysfunction by allowing direct delivery of desaturated venous blood to the left atrium. In these patients, a Pao_2 of 40 to 50 mm Hg and a Sao_2 of 70% to 80% are acceptable until RV function improves over the course of days.

DiNardo JA. Anesthesia for congenital heart disease. In: DiNardo JA, Zvara DA, eds. *Anesthesia for Cardiac Surgery*. 3rd ed. Oxford: Blackwell Publishing; 2008:167–251.

D.3. Following placement of a modified Blalock-Taussig shunt (MBTS) for TOF/PS in an infant, what Sao_2 is acceptable?

As illustrated in Figure 38.5B in the presence of some antegrade pulmonary blood flow, an appropriate Sao_2 would be 80% to 90%. In the absence of any antegrade pulmonary blood flow, single ventricle physiology would exist and a Sao_2 of 70% to 80% would be more appropriate. Sao_2 is determined by the relative volumes and saturations of recirculated systemic venous blood and effective systemic blood flows that have mixed and reached the aorta. This is summarized in the following equation:

$$\text{Aortic } Sao_2 = \frac{\begin{array}{c}\text{([pulmonary venous saturation] [effective systemic blood flow]}\\ \text{+ [systemic venous saturation] [recirculated systemic venous blood flow])}\end{array}}{\text{(total systemic blood flow)}}.$$

This is demonstrated in Figure 38.5B where the $Sao_2 = [(98)(1) + (65)(0.5)]/1 = 87$
Three variables will ultimately affect Sao_2:

1. *The ratio of total pulmonary to total systemic blood flow ($Q_P : Q_S$).* A greater proportion of the arterial blood will consist of saturated blood (pulmonary venous blood) than of desaturated blood (systemic venous blood) when $Q_P : Q_S \geq 1{:}1$. $Q_P : Q_S$ will be increased when systemic arterial blood pressure is high and PVR is low.
2. *Systemic venous saturation.* For a given $Q_P : Q_S$ and pulmonary venous saturation, a decrease in systemic venous saturation will result in a decreased arterial saturation. Decreases in systemic venous saturation occur as the result of decreases in systemic oxygen delivery or increases in systemic oxygen consumption. Recall that systemic oxygen delivery is the product of systemic blood flow and arterial oxygen content. Arterial oxygen content, in turn, is dependent on the hemoglobin concentration and the arterial saturation. Efforts should be made to increase hematocrit into the range of 35% to 45%, cardiac output should be enhanced with inotropes (dopamine, 5 to 10 μg/kg/minute), and systemic O_2 consumption reduced by appropriate levels of sedation/anesthesia and muscle relaxation if necessary.
3. *Pulmonary venous saturation*. In the absence of large intrapulmonary shunts and/or $\dot{V}/\dot{Q}$ mismatch, pulmonary venous saturation should be close to 100% breathing room air. In the presence of pulmonary parenchymal disease, pulmonary venous saturation may be reduced. The $\dot{V}/\dot{Q}$ mismatch component of pulmonary venous

desaturation will be largely eliminated with a FIO_2 of 1.0, while the intrapulmonary shunt contribution will not be eliminated. For any given systemic venous saturation and $Q_P : Q_S$, a reduction in pulmonary venous saturation will result in a decreased arterial saturation.

DiNardo JA. Anesthesia for congenital heart disease. In: DiNardo JA, Zvara DA, eds. *Anesthesia for Cardiac Surgery*. 3rd ed. Oxford: Blackwell Publishing; 2008:167–251.

D.4. What is junctional ectopic tachycardia (JET)?

Postoperative JET is a transient tachyarrhythmia that occurs immediately following congenital heart surgery. A much rarer form of congenital JET exists as well. JET is due to enhanced automaticity in the area of the atrioventricular (AV) node or proximal His bundle. Associated with JET is a higher than average incidence of AV block. The incidence of JET following TOF/PS repair may be as high as 20% and is felt to be secondary to surgical trauma in the area of the AV node secondary to the retraction necessary to expose the VSD and RVOT from across the tricuspid valve.

JET typically manifests with a junctional rate only slightly faster than the sinus node rate and is the only narrow complex tachycardia in which the atrial rate is less than the ventricular rate (A : V ratio <1:1). Much less commonly (10%), there may be retrograde activation of the atrium with inverted P waves noted and A : V ratio = 1:1. In either case, there is loss of AV synchrony (loss of atrial kick). In many instances, this arrhythmia is well tolerated. However, JET with heart rate greater than 170 bpm is associated with hemodynamic instability and increased postoperative mortality.

Cardioversion is ineffective as is adenosine. The most effective therapy for treatment of JET is atrial pacing at a rate slightly faster than the junctional rate such that A-V synchrony is reinitiated. This therapy is effective unless the junctional rate is very fast (>160 to 170 bpm), at which point atrial pacing at a faster rate is unlikely to improve hemodynamics because the reinitiation of A-V synchrony is offset by the dramatic reduction in diastolic filling time present at these rates. In this circumstance, the most effective therapy is multimodal. JET requiring aggressive treatment prolongs postoperative ventilation times and intensive care unit stay. The goal of aggressive therapy is to terminate JET or reduce the rate to point where atrial pacing can be reinitiated. In order, the following modalities are applied:

- Fever is aggressively treated with antipyretics.
- Sedation and hemodynamics are optimized.
- Reduction of inotrope doses is useful because most agents have chronotrophic activity. This may be difficult in the setting of hemodynamic instability and low cardiac out put syndrome.
- Mild systemic hypothermia is introduced. A cooling blanket and icepacks are used to reduce patient temperature to 32° C (89.6° F) to 35° C (95° F). This usually requires sedation and paralysis to prevent shivering.
- Procainamide or amiodarone therapy is initiated.

Walsh EP. Automatic atrial and junctional tachycardias. In: Walsh EP, Saul JP, Triedman JK, eds. *Cardiac Arrhythmias in Children and Young Adults with Congenital Heart Disease*. Philadelphia: Lippincott Williams & Wilkins; 2001:115–135.

CHAPTER 39

Transposition of the Great Arteries

JAMES A. DINARDO

A 3-DAY-OLD, FULL-TERM, 3.4-KG NEWBORN is scheduled for an arterial switch operation (ASO). Shortly after birth, he demonstrated reverse differential cyanosis with a right arm arterial saturation of 40% and a lower extremity saturation of 60% despite prostaglandin E_1. A bedside balloon atrial septostomy was performed with resolution of reverse differential cyanosis and improvement of arterial saturation to 75%. Prostaglandin E_1 was discontinued 4 hours after the septostomy. He is extubated receiving 0.5 L per minute supplemental O_2 through nasal cannula. His arterial oxygen saturation is 75%; blood pressure, 63/37 mm Hg; pulse, 145 beats per minute; respiration, 46 breaths per minute.

A. Medical Disease and Differential Diagnosis

1. What is transposition of the great arteries (D-TGA)?
2. What additional cardiac lesions are associated with D-TGA?
3. What is the natural history of D-TGA?
4. What is the pathophysiology of D-TGA?
5. What determines the oxygen saturation in patients with D-TGA?
6. Why did this infant have reverse differential cyanosis?
7. What are the preoperative issues pertaining to the coronary arteries in D-TGA?
8. What are the clinical subsets of D-TGA?
9. What is the differential diagnosis of D-TGA and how is the diagnosis made?
10. What preoperative interventions can help stabilize a patient with D-TGA?
11. What are the surgical options for repair? Why is one chosen over the others?

B. Preoperative Evaluation and Preparation

1. What information is important to prepare for this case?
2. What are the anesthetic goals before cardiopulmonary bypass (CPB)?
3. What is the plan for glucose management in this patient?

C. Intraoperative Management

1. How would you monitor this infant?
2. What would be the best method of induction?
3. Is CPB in infants and children different from adults?
4. What is modified ultrafiltration (MUF)?
5. Briefly describe the surgical techniques of the Mustard/Senning, ASO, and Rastelli procedures.
6. What is hypothermia and how is it classified? What is low-flow cardiopulmonary bypass (LFCPB)? What is deep hypothermic circulatory arrest (DHCA)?
7. Why is hypothermia beneficial to the brain during LFCPB and DHCA?
8. Explain the difference between α-stat and pH-stat blood gas management.
9. What are the immediate post-CPB issues following ASO?

D. Postoperative Management

1. How is myocardial ischemia addressed in the intensive care unit (ICU) following the ASO?
2. What immediate postoperative problems would be anticipated following the Rastelli procedure?
3. What intermediate and long-term surgical problems are seen after ASO?
4. What are the long-term outcomes after ASO?
5. What are the long-term outcomes after Rastelli repair for D-TGA with left ventricular outflow tract (LVOT) obstruction?
6. What is long-term neurologic outcome like after ASO?

A. Medical Disease and Differential Diagnosis

A.1. What is transposition of the great arteries (D-TGA)?

D-TGA refers specifically to the anatomic circumstance wherein there is concordance of the atrioventricular (AV) connections associated with discordance of the ventriculoarterial connections. By far the most common manifestation of this anatomy occurs in patients with [S,D,D] segmental anatomy, also known as *D-TGA*. There is atrial situs solitus, D-loop ventricles, and D-loop great arteries. A right-sided right atrium (RA) connects through a right-sided tricuspid valve and right ventricle (RV) to a right-sided and anterior aorta. A left-sided left atrium (LA) connects through a left-sided mitral valve and left ventricle (LV) to a left-sided and posterior pulmonary artery (PA). As a result, there is fibrous continuity between the mitral and pulmonic valves with a lack of fibrous continuity (conus) between the tricuspid and aortic valves. In D-TGA, the combination of AV concordance (RA to RV; LA to LV) and ventriculoarterial discordance (RV to aorta; LV to PA) produces a parallel rather than a normal series circulation.

DiNardo JA. Anesthesia for congenital heart surgery. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart Disease*. London: Arnold; 2004:45–65.

DiNardo JA. Transposition of the great vessels. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2005:357–380.

A.2. What additional cardiac lesions are associated with D-TGA?

The most commonly associated cardiac anomalies are a persistent patent foramen ovale (PFO), patent ductus arteriosus (PDA), ventricular septal defect (VSD), and subpulmonic stenosis or LVOT obstruction. Approximately 50% of patients with

D-TGA will present with a PDA before prostaglandin E_1 administration. The foramen ovale is almost always patent, but a true secundum atrial septal defect (ASD) exists in only approximately 5% of patients. Although angiographically detectable VSDs may occur in 30% to 40% of patients, only approximately one-third of these defects are hemodynamically significant. Therefore, for practical purposes, 75% of patients have an intact ventricular septum (IVS). LVOT obstruction is present in approximately 30% of patients with VSD and is most often due to an extensive subpulmonary fibromuscular ring or posterior malposition of the outlet portion of the ventricular septum.

Paul M. Complete transposition of the great arteries. In: Adams FH, Riemenschneider TA, eds. *Fetal and Neonatal Cardiology*. Philadelphia: WB Saunders; 1989:471–423.

A.3. What is the natural history of D-TGA?

D-TGA is a common congenital heart lesion accounting for 5% to 7% of all congenital cardiac defects, second in frequency only to isolated VSDs. Without intervention, D-TGA has a high mortality rate: 45% will die within the first month and 90% will die within the first year of life. This is particularly unfortunate, because infants with D-TGA rarely have extracardiac defects. Advancements in medical and surgical therapy in the last 20 years have greatly improved the outlook for these infants. In fact, following stabilization with prostaglandin E_1 and the Rashkind-Miller balloon septostomy, many of these infants can be offered a definite surgical procedure (arterial switch), giving them a quality of life similar to that of normal children.

Hypoxia and intractable congestive heart failure (CHF) are the two primary causes of death. The early onset and progression of pulmonary vascular occlusive disease (PVOD) plays a major role in the dismal outlook in these patients. Compared with other forms of congenital heart disease, infants with transposition of great vessels (TGV) are at particular risk for accelerated development of PVOD. Systemic hypoxemia, the presence of bronchopulmonary collaterals (which deliver deoxygenated blood to the precapillary pulmonary arterioles), platelet aggregation in the lung, and polycythemia have all been implicated. Infants with TGV and large VSD without LVOT obstruction are at an even higher risk for the early development of PVOD due to exposure of the pulmonary vascular bed to high blood flow and systemic pressures. Advanced, nonreversible pulmonary hypertension reduces the corrective surgical options available to the patient.

DiNardo JA. Transposition of the great vessels. In: Lake CL, Booker, PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2005:357–380.

A.4. What is the pathophysiology of D-TGA?

In the parallel arrangement of D-TGA, deoxygenated systemic venous blood recirculates through the systemic circulation without reaching the lungs to be oxygenated. This recirculated systemic venous blood represents a physiologic right-to-left shunt. Likewise, oxygenated pulmonary venous blood recirculates uselessly through the pulmonary circulation. This recirculated pulmonary venous blood represents a physiologic left-to-right shunt. Therefore, in a parallel circulation, the physiologic shunt or the percentage of venous blood from one system that recirculates in the arterial outflow of the same system is 100% for both circuits. Unless there are one or more communications between the parallel circuits to allow intercirculatory mixing, this arrangement is not compatible with life.

The sites available for intercirculatory mixing in D-TGA can be intracardiac (PFO, ASD, VSD) or extracardiac (PDA, bronchopulmonary collaterals). Several factors affect the amount of intercirculatory mixing. The number, size, and position of anatomic communications are important. One large, nonrestrictive communication will provide better mixing than two or three restrictive communications. Reduced ventricular compliance and elevated systemic and pulmonary vascular resistance (PVR) tend to reduce intercirculatory mixing by impeding flow across the anatomic communications.

The position of the communication is also important. Poor mixing occurs even with large anterior muscular VSDs due to their unfavorable position. Finally, in the presence of adequate intercirculatory mixing sites, the extent of intercirculatory mixing is directly related to total pulmonary blood flow. Patients with reduced pulmonary blood flow secondary to subpulmonary stenosis or PVOD will have reduced intercirculatory mixing.

DiNardo JA. Anesthesia for congenital heart surgery. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart Disease*. London: Arnold; 2004:45–65.

DiNardo JA. Transposition of the great vessels. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2005:357–380.

A.5. What determines the oxygen saturation in patients with D-TGA?

In D-TGA, intercirculatory mixing is the result of anatomic right-to-left and anatomic left-to-right shunts that are equal in magnitude. The anatomic right-to-left shunt produces effective pulmonary blood flow, which is the volume of systemic venous blood reaching the pulmonary circulation. The anatomic left-to-right shunt produces an effective systemic blood flow, which is the volume of pulmonary venous blood reaching the systemic circulation. Effective pulmonary blood flow, effective systemic blood flow, and the volume of intercirculatory mixing are always equal. The systemic blood flow is the sum of recirculated systemic venous blood plus effective systemic blood flow. Likewise, total pulmonary blood flow is the sum of recirculated pulmonary venous blood plus effective pulmonary blood flow. Recirculated blood makes up the largest portion of total pulmonary and systemic blood flow, with effective blood flows contributing only a small portion of the total flows. This is particularly true in the pulmonary circuit where the total pulmonary blood flow (Q_P) and the volume of the pulmonary circuit (LA, LV, PA) is three to four times larger than the total systemic blood flow (Q_S) and the volume of the systemic circuit (RA, RV, aorta). The net result is production of a transposition physiology, where the PA oxygen saturation is greater than the aortic oxygen saturation. Figure 39.1 further elucidates these concepts.

Arterial saturation (Sao_2) is determined by the relative volumes and saturations of the recirculated systemic and effective systemic blood flows reaching the aorta. This is summarized in the following equation:

$$\text{Aortic saturation} = \frac{\begin{array}{c}([\text{systematic venous saturation}]\,[\text{recirculated systemic blood flow}] \\ +\,[\text{pulmonary venous saturation}]\,[\text{effective systemic blood flow}])\end{array}}{(\text{total sytemic blood flow})}$$

This is illustrated in Figure 39.1 where:

$$Sao_2 = ([50][1.2] + [99][1.1])/\,2.3 = 73\%$$

Obviously, the greater the effective systemic blood flow (intercirculatory mixing) relative to the recirculated systemic blood flow, the greater the aortic saturation. For a given amount of intercirculatory mixing and total systemic blood flow, a decrease in systemic venous or pulmonary venous saturation will result in a decrease in arterial saturation.

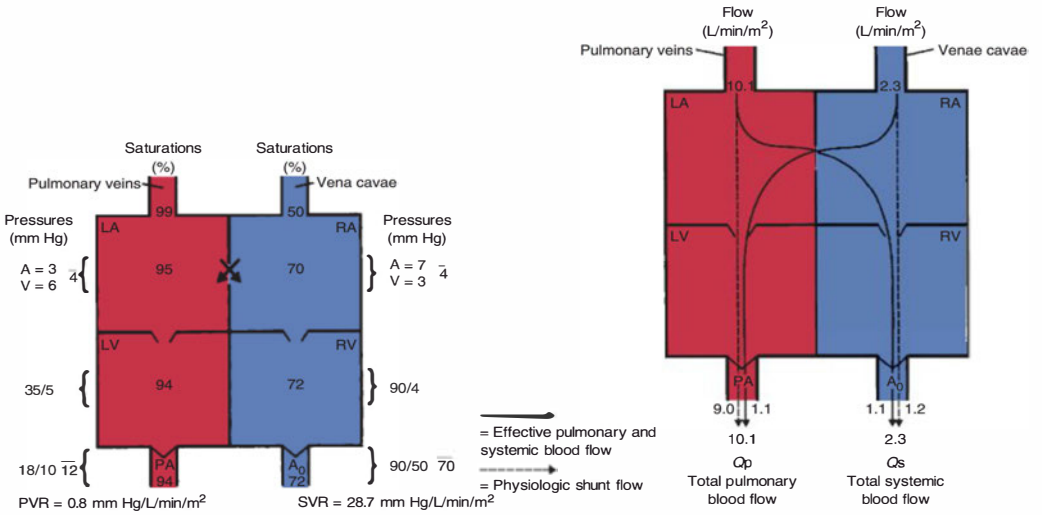

Figure 39.1 Depiction of saturations, pressures, and blood flows in complete transposition of the great vessels with intercirculatory mixing at the atrial level and a small left ventricular outflow tract gradient. It is apparent that total pulmonary blood flow (10.1 L/min/m²) is almost five times the total systemic blood flow (2.3 L/min/m²). Effective (EFF) pulmonary and effective systemic blood flow are equal (1.1 L/min/m²) and are the result of an anatomic shunt at the atrial level. The physiologic left-to-right shunt is 9 L/min/m²; this represents blood recirculated from the pulmonary veins to the pulmonary artery. The physiologic right-to-left shunt is 1.2 L/min/m²; this represents blood recirculated from the systemic veins to the aorta. In this depiction, pulmonary vascular resistance is low (approximately 1/35 of systemic vascular resistance) and there is a small (17 mm peak to peak) gradient from the left ventricle to the pulmonary artery. These findings are compatible with the high pulmonary blood flow depicted. LA, left atrium; LV, left ventricle; PA, pulmonary artery; PVR, pulmonary vascular resistance; *Qp*, total pulmonary blood flow; *Qs*, total systemic blood flow; RA, right atrium; RV, right ventricle; SVR, systemic vascular resistance. (Modified from Freed MO, Keane JF. Profiles in congenital heart disease. In: Grossman W, ed. *Cardiac Catheterization and Angiography*. Philadelphia: Lea & Febiger; 1986:463, with permission.)

DiNardo JA. Anesthesia for congenital heart surgery. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart Disease*. London: Arnold; 2004:45–65.

DiNardo JA. Transposition of the great vessels. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2005:357–380.

A.6. Why did this infant have reverse differential cyanosis?

In D-TGA with IVS, the anatomic mixing sites are usually a PDA and a PFO. The dynamics of intercirculatory mixing in D-TGA with IVS are complex. Anatomic shunting at the atrial level is ultimately determined by the size of the atrial communication and the cyclic pressure variations between the left and right atria. The volume and compliance of the atria, ventricles, and vascular beds in each circuit, as well as heart rate (HR) and phase of respiration all influence this relationship. Shunting is from the RA to the LA during diastole as the result of the reduced ventricular and vascular compliance of the

systemic circuit (RV and systemic arterial circuit). In systole, shunt is from the LA to the RA primarily because of the large volume of blood returning to the LA as a result of the high volume of recirculated pulmonary blood flow.

The direction of shunting across the PDA largely depends on the PVR and the size of the intra-atrial communication. When the PVR is low and the intra-atrial communication is nonrestrictive, shunting is predominantly from the aorta to the PA through the PDA (effective pulmonary blood flow) and predominantly from the LA to RA across the atrial septum (effective systemic blood flow). When PVR is elevated, shunting across the PDA is likely to be bidirectional that in turn encourages bidirectional shunting across the atrial septum. When PVR is high and PA pressure exceeds aortic pressure shunting at the PDA will be predominantly from the PA to the aorta. This will create reverse differential cyanosis—physiology wherein the preductal arterial saturation (right arm) is lower than the postductal arterial saturation (legs). This physiology is usually the result of a restrictive atrial communication producing left atrial hypertension and is associated with low effective blood flows (poor mixing) and hypoxemia. A balloon atrial septostomy can be lifesaving in this setting. Decompression of the LA promotes mixing at the atrial level and also reduces PVR and PA pressure promoting mixing at the PDA. Other causes of reverse differential cyanosis to be considered in D-TGA are the presence of an interrupted aortic arch or severe aortic coarctation.

DiNardo JA. Anesthesia for congenital heart surgery. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart Disease*. London: Arnold; 2004:45–65.

DiNardo JA. Transposition of the great vessels. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2005:357–380.

A.7. What are the preoperative issues pertaining to the coronary arteries in D-TGA?

As in normally related great vessels, the coronary arteries in D-TGA arise from the aortic sinuses that face the PA. In normally related vessels, these sinuses are located on the anterior portion of the aorta, whereas in D-TGA, they are located posteriorly. In most D-TGA patients (70%), the right sinus is the origin of the right coronary artery, whereas the left sinus is the origin of the left main coronary artery. In the remainder of cases, there is considerable variability, with the most common variations being shown in Figure 39.2.

Most patients with D-TGA have a coronary anatomy that is suitable for the coronary reimplantation necessary in the ASO. Patients with certain types of coronary anatomy (intramural coronaries, single coronary artery) are at risk for postoperative myocardial ischemia and early mortality because reimplantation can result in the distortion of the coronary ostia or the narrowing of the artery itself. Patients with intramural coronaries generally require resuspension of the posterior leaflet of neopulmonary valve once the coronaries and a surrounding tissue cuff are excised.

The presence of a single coronary artery or intramural coronary arteries is a risk factor for mortality and this risk has persisted over the last two decades.

DiNardo JA. Transposition of the great vessels. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2005:357–380.

A.8. What are the clinical subsets of D-TGA?

Four clinical subsets based on anatomy, pulmonary blood flow, and intercirculatory mixing can be used to characterize patients with D-TGA. These are summarized in Table 39.1.

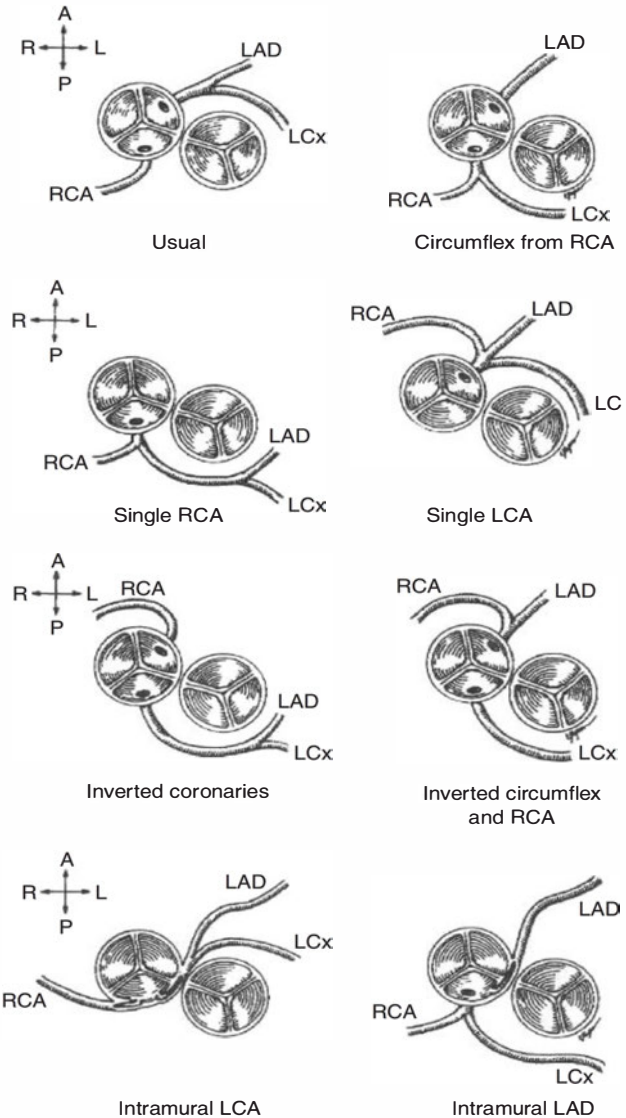

Figure 39.2 Depiction of the most common coronary artery patterns in transposition of the great vessels. The aorta is depicted anterior and to the right of the pulmonary artery. LAD, left anterior descending coronary artery; LCA, left coronary artery; LCx, left circumflex coronary artery; RCA, right coronary artery. (Adapted from Mayer JE, Sanders SP, Jonas RA, et al. Coronary artery pattern and outcome of arterial switch operation for transposition of the great arteries. *Circulation.* 1990:82(suppl III):144, with permission.)

Table 39.1 Clinical Subsets of Transposition of Great Arteries

ANATOMY	PULMONARY BLOOD FLOW	INTERCIRCULATORY MIXING
D-TGA with IVS	Increased	Small
D-TGA with IVS; nonrestrictive atrial septum or PDA	Increased	Large
D-TGA with VSD	Increased	Large
D-TGA with VSD and LVOT obstruction	Reduced	Small
D-TGA with PVOD	Reduced	Small

D-TGA, transposition of great arteries; IVS, intact ventricular septum; PDA, patent ductus arteriosus; VSD, ventricular septal defect; LVOT, left ventricular outflow tract; PVOD, pulmonary vascular occlusive disease.
DiNardo JA. Transposition of the great vessels. In: Lake CL, Booker, PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2005:357–380.

A.9. What is the differential diagnosis of D-TGA and how is the diagnosis made?

Figure 39.3 delineates the differential diagnosis for D-TGA in the cyanotic newborn.

D-TGA may be associated with either cyanosis or CHF. In patients in whom intercirculatory mixing is limited, cyanosis is severe with little evidence of CHF. CHF is the more common finding in patients with increased pulmonary blood flow, a large quantity of intercirculatory mixing, and mild cyanosis.

Chest radiographs may appear normal in the first few weeks of life in infants with D-TGA and IVS. Eventually, the triad of an enlarged egg-shaped heart (large RA and RV), narrow superior mediastinum, and increased pulmonary vascular markings evolve. In patients with D-TGA and VSD without LVOT obstruction, a large cardiac silhouette and prominent pulmonary vascular markings are seen at birth. Right axis deviation and right ventricular hypertrophy are the electrocardiographic (ECG) findings in D-TGA with IVS, whereas right axis deviation, left ventricular hypertrophy, and right ventricular hypertrophy are seen with D-TGA and VSD.

Two-dimensional echocardiography is the diagnostic modality of choice in the diagnosis and assessment of infants with D-TGA. It accurately establishes the diagnosis of D-TGA and reliably identifies associated abnormalities such as VSD, mitral and tricuspid valve abnormalities, and LVOT obstruction. It also reliably delineates coronary artery anatomy. Echocardiographic analysis of the ventricular septal position or LV geometry is also used to noninvasively assess the LV to RV pressure ratio and IV mass in neonates with D-TGA and IVS who are being evaluated as candidates for an ASO.

In institutions with high-level echocardiography, a comprehensive cardiac catheterization is no longer routinely performed in neonates with D-TGA. A limited catheterization may be performed in conjunction with a balloon atrial septostomy. In the rare instance where coronary anatomy cannot be clearly delineated by echocardiography, coronary angiography may be indicated. During catheterization of infants with PVOD, a trial of ventilation at an FIO_2 of 1.0 may be used to determine whether PVR is fixed or remains responsive to oxygen-induced pulmonary vasodilatation.

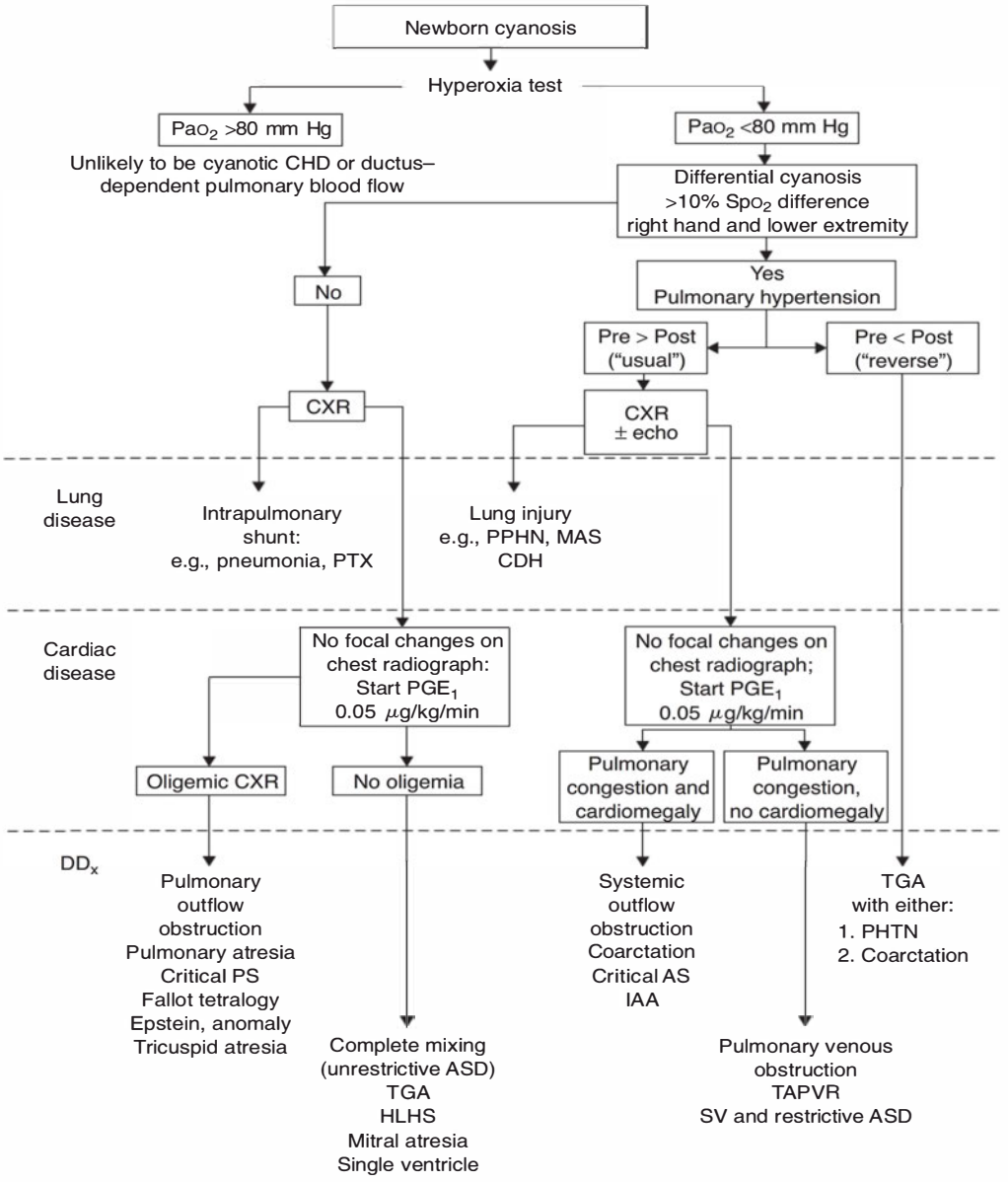

Figure 39.3 The differential diagnosis of transposition of the great arteries. AS, aortic stenosis; ASD, atrial septal defect; CHD, congenital heart disease; CXR, chest radiograph; HLHS, hypoplastic left heart syndrome; IAA, interrupted aortic arch; MAS, meconium aspiration syndrome; PHTN, pulmonary hypertension; PPHN, persistent pulmonary hypertension of the newborn; PS, pulmonary stenosis; PTX, pneumothorax; SV, single ventricle; TAPVR, total anomalous pulmonary venous return; TGA, transposition of great arteries; CDH, congenital diaphragmatic hernia.

DiNardo JA. Anesthesia for congenital heart surgery. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart Disease*. London: Arnold; 2004:45–65.

DiNardo JA. Transposition of the great vessels. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2005:357–380.

A.10. What preoperative interventions can help stabilize a patient with D-TGA?

Intact ventricular septum

Most neonates with D-TGA and IVS will be hypoxemic (arterial saturation ≤60%) within the first day of life. A proportion of these patients will have severely reduced effective pulmonary and systemic blood flow resulting in a Pao_2 less than 20 mm Hg, hypercarbia, and an evolving metabolic acidosis secondary to the poor tissue oxygen delivery. Prostaglandin E_1 (0.01 to 0.05 μg/kg/minute) is administered to dilate and maintain the patency of the ductus arteriosus. This will be effective in increasing effective pulmonary and systemic blood flow, and in improving Pao_2 and tissue oxygen delivery *if* (1) PVR is less than systemic vascular resistance (SVR) and (2) there is a nonrestrictive or minimally restrictive atrial septal communication. In some centers, all neonates stabilized on prostaglandin E_1 alone have a balloon atrial septostomy to enlarge the atrial septal communication so that prostaglandin E_1 can be stopped and surgery scheduled on a semielective basis. Prostaglandin E_1 infusion is associated with apnea, pyrexia, fluid retention, and platelet dysfunction.

If prostaglandin E_1 does not improve tissue oxygen delivery, then an emergent balloon atrial septostomy is performed in the catheterization laboratory utilizing angiography or in the ICU utilizing echocardiography. These patients also require tracheal intubation and mechanical ventilation. This allows reduction of PVR through induction of a respiratory alkalosis and elimination of pulmonary ventilation/pefusion ($\dot{V}/\dot{Q}$) mismatch. Sedation and muscle relaxation reduce oxygen consumption, thereby increasing mixed venous O_2 saturation. Recall that for a given amount of intercirculatory mixing and total systemic blood flow, an increase in systemic venous or pulmonary venous saturation will result in an increase in arterial saturation.

In rare instances, the combination of prostaglandin E_1, an atrial septostomy, and mechanical ventilation with sedation/muscle relaxation may be ineffective. In this circumstance, extracorporeal membrane oxygenation (either venoarterial or venovenous) support to improve tissue oxygenation and to reverse end-organ insult and lactic acidosis before surgery is an alternative approach to emergent surgery in a critically ill neonate.

Ventricular septal defect

Infants in this subset are mildly cyanotic with symptoms of CHF. Pulmonary blood flow is increased, and there is extensive intercirculatory mixing. Reducing PVR to further augment pulmonary blood flow and intercirculatory mixing will not greatly influence the systemic oxygenation. Reducing PVR in these patients may increase the recirculated volume in the pulmonary circuit by increasing circuit compliance. Maintaining systemic blood flow will then necessitate an increase in cardiac output from a failing heart. These patients are commonly stable enough not to require immediate surgical or catheterization laboratory intervention. They are, however, candidates for an ASO before intractable CHF or advanced PVOD occurs.

Ventricular septal defect and left ventricular outflow tract obstruction

The degree of cyanosis in these infants will depend on the extent of LVOT obstruction. LVOT obstruction reduces pulmonary blood flow and intercirculatory mixing, and it protects the pulmonary vasculature from the increased pressures and volumes that accelerate the development of PVOD. The more severe the LVOT obstruction, the less effective will be the efforts to increase pulmonary blood flow by decreasing PVR. When LVOT obstruction is severe, the infant is severely cyanotic and progressively develops polycythemia. These infants may require a palliative aortopulmonary shunt to increase pulmonary blood flow. Ideally, a definitive repair in the form of a Rastelli procedure is performed in the neonatal period.

Pulmonary vascular occlusive disease

The goal of diagnosis and treatment of infants with D-TGA is to intervene surgically before the development of PVOD. As PVOD advances, the child becomes progressively cyanotic and polycythemic. Efforts to reduce PVR will increase pulmonary blood flow and intercirculatory mixing in infants where PVR is not fixed. Infants with advanced PVOD (PVR >10 Wood units; histologic grade 4) are generally candidates only for palliative therapy. In particular, closure of a VSD in the presence of advanced pulmonary hypertension carries a high mortality rate owing to the afterload mismatch and the resultant pulmonary ventricular (LV) dysfunction. These patients are candidates for a palliative intra-atrial physiologic repair (Mustard or Senning procedure) without closure or with fenestrated closure (4- to 5-mm hole in the center of the VSD patch) of the VSD.

DiNardo JA. Anesthesia for congenital heart surgery. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart Disease*. London: Arnold; 2004:45–65.

DiNardo JA. Transposition of the great vessels. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2005:357–380.

A.11. What are the surgical options for repair? Why is one chosen over the others?

Arterial anatomic repair: arterial switch (Jatene) operation

The ASO anatomically corrects the discordant ventriculoarterial connections and is the procedure of choice for patients with D-TGA. Following repair, the RV is connected to the PA and the LV to the aorta. Clinical success with the ASO, summarized in Figure 39.4, was achieved in 1975. In order for the ASO to be successful, the original pulmonary ventricle (LV) must have sufficient mass to be capable of functioning as the systemic ventricle following the switch. Patient selection and the timing of the surgical procedure are, therefore, important variables in determining the success of this procedure. The ASO was originally described in patients with D-TGA and a large VSD or a large PDA. In these patients, the pulmonary ventricle (LV) remains exposed to systemic pressures, and the LV mass remains sufficient to support the systemic circulation. For this subset of patients, the ASO is generally performed within the first 2 to 3 months of life, before intractable CHF or irreversible PVOD intervene.

In patients with D-TGA and IVS, there is a progressive reduction in LV mass as the physiologic pulmonary hypertension present at birth resolves progressively over the first weeks following birth. Adequate LV mass to support the systemic circulation reliably exists in these patients for only the first 3 or 4 weeks following birth. In patients with D-TGA and IVS, the ASO can be performed primarily or as the second

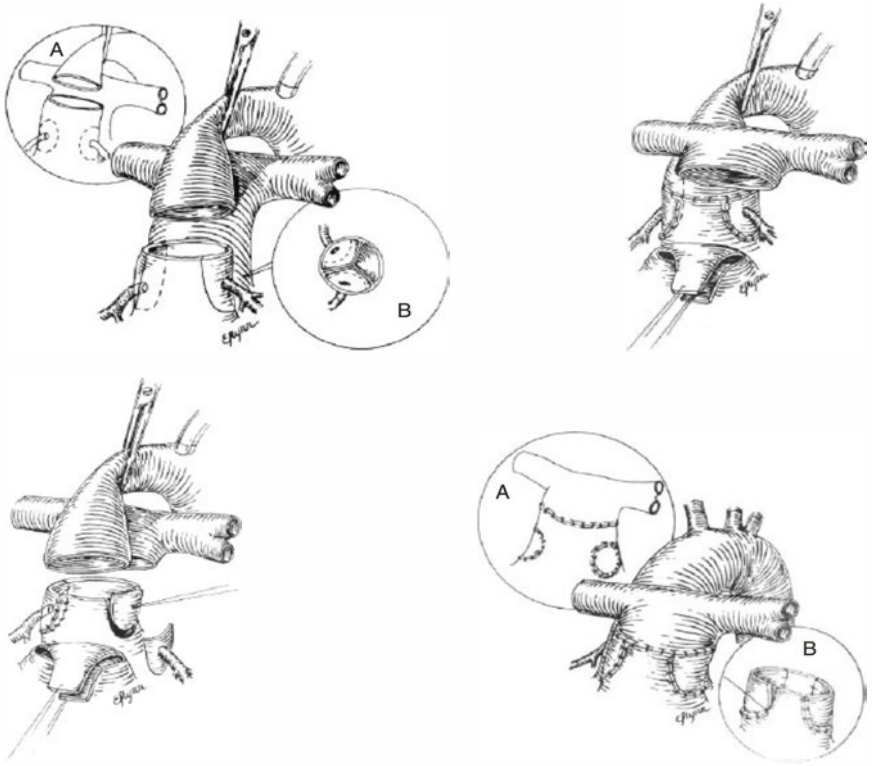

Figure 39.4 Details of the arterial switch procedure. **Upper left.** Aorta is transected and left and right main coronary arteries are excised using **(A)** either button of aortic wall or **(B)** segment of aortic wall extending from rim of aorta. **Lower left.** Equivalent segment of pulmonary arterial wall is excised, and coronary arteries are sutured to pulmonary artery. **Upper right.** Distal pulmonary artery is brought anterior to ascending aorta (LeCompte maneuver), and proximal pulmonary artery is anastomosed to distal aorta. **Lower right.** Sites of coronary explantation are repaired using either **(A)** patch of prosthetic material or **(B)** segment of pericardium. Finally, proximal aorta is sutured to distal pulmonary artery. (Adapted from Castanda AR, Norwood WI, Jonas RA, et al. Transposition of the great arteries and intact ventricular septum: anatomical repair in the neonate. *Ann Thorac Surg.* 1984;38:438–443)

phase of a staged procedure. A successful primary ASO must generally be performed within the first 4 weeks of life; most are performed in the first few days of life. Previously, favorable candidates for the procedure in the neonatal period were shown to have an LV to RV pressure ratio of at least 0.6 by catheterization. Currently, two-dimensional echocardiography is used to noninvasively assess the LV to RV pressure ratio. Three types of ventricular septal geometry have been described. Patients in whom the ventricular septum bulges to the left (type 3), indicating a low pressure in the pulmonary ventricle (LV), are not candidates for a neonatal ASO. Patients with septal bulging to the right (type 1), indicating a high pressure in the pulmonary ventricle (LV), and those patients with an intermediate septal position (type 2) are considered good candidates. Most neonates with D-TGA and IVS who are suitable candidates for an ASO have type 2 septal geometry.

The staged ASO for D-TGA with IVS is used for those neonates in whom surgery cannot be performed in the first month of life secondary to events such as prematurity, sepsis, low birth weight (<1.0 kg), or late referral. The staged procedure retrains the LV to accept the systemic workload. The preparatory surgery involves creation of a nonrestrictive atrial septum (if it does not already exist), placement of a PA band, and creation of an aortopulmonary shunt with entry to the PA distal to the band. The band must be tight enough to increase pressure in the pulmonary ventricle (LV) to approximately one-half to two-thirds of that in the systemic ventricle (RV). This will increase the afterload sufficiently to stimulate an increase in LV mass. Historically, after 3 to 6 months, the PA was debanded, the shunt taken down, and an ASO performed. Currently a rapid two-stage repair is undertaken in which the ASO is performed as early as 1 week after preparatory PA banding, often during the same hospitalization. This approach is based on the fact that a doubling of LV mass is seen after 1 week of PA banding. The staged procedure is complicated by the fact that the adjustment of the PA band to the proper tightness is not an easy task and that the PA band and systemic to PA shunt may result in a distortion of the PA, making the definite ASO difficult. Intraoperative transesophageal echocardiography (TEE) is useful in guiding placement of the PA band. The band is tightened enough to flatten the intraventricular septum by shifting it toward the RV.

Intra-atrial physiologic repairs: Mustard and Senning procedures

Both the Mustard and the Senning procedures are atrial switch procedures that surgically create discordant AV connections in D-TGA. Systemic venous blood is routed to the LV and the PA, whereas pulmonary venous blood is routed to the RV and the aorta. This arrangement results in physiologic but not anatomic correction of D-TGA as the morphologic RV becomes the systemic ventricle. Given the current success with and the almost universal application of the more definitive ASO, these intra-atrial switch procedures are primarily of historic interest in patients with D-TGA.

Rastelli procedure

The Rastelli procedure was described in 1969 as a method of anatomically correcting D-TGA with VSD and LVOT obstruction. This surgery is used when LVOT obstruction in the form of subpulmonic and/or pulmonic stenosis is surgically uncorrectable. Performance of an ASO under these circumstances would leave the infant with residual LVOT obstruction (aortic or subaortic stenosis).

DiNardo JA. Transposition of the great arteries. In: Jonas RA, ed. *Comprehensive Surgical Management Of Congenital Heart Disease*. London: Arnold; 2004:256–278.

B. Preoperative Evaluation and Preparation

B.1. What information is important to prepare for this case?

The preoperative evaluation should begin with a careful history and physical examination. Gestational age, birth complications, family history, and any other medical problems should be noted. A comprehensive airway evaluation should be performed and the previous endotracheal tube size and leak pressure noted. Arterial and intravenous access should be assessed. A type and cross must be sent to the blood bank to ensure adequate red cells and blood component therapies are available in the operating room (OR).

The preoperative ECG and chest radiograph should be reviewed. The preoperative echocardiograms should be reviewed. Particular attention should be paid to septal

geometry, biventricular function, coronary anatomy, and adequacy of mixing at the atrial septal and ductal levels. Prostaglandin E_1 was discontinued in the patient but the ductus arteriosus may remain patent.

Laboratory data should include a complete blood count, electrolytes, platelet count, arterial blood gas, calcium, blood urea nitrogen, creatinine, liver function tests and glucose. Given that this infant presented with severe hypoxemia, end-organ dysfunction must be ruled out. The liver function tests and creatinine should be normal; if they are elevated, consideration should be given to further medical optimization. A head ultrasonographic examination should be performed to rule out intraventricular hemorrhage.

DiNardo JA. Anesthesia for congenital heart surgery. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart Disease.* London: Arnold; 2004:45–65.

B.2. What are the anesthetic goals before cardiopulmonary bypass (CPB)?

- Maintain HR, contractility, and preload to maintain cardiac output; decreases in cardiac output decrease systemic venous saturation with a resultant fall in arterial saturation.
- Maintain ductal patency with prostaglandin E_1 (0.01 to 0.05 μg/kg/minute) in ductal-dependent patients.
- Avoid increases in PVR relative to SVR; increases in PVR will decrease pulmonary blood flow and reduce intercirculatory mixing; in patients with PVOD, ventilatory interventions should be used to reduce PVR; in patients with LVOT obstruction that is not severe, ventilatory interventions to reduce PVR increase pulmonary blood flow and intercirculatory mixing.
- Reductions in SVR relative to PVR should be avoided; decreased SVR increases recirculation of systemic venous blood and decreases arterial saturation.
- In patients with D-TGA and VSD with symptoms of CHF, ventilatory interventions to reduce PVR are not warranted because they will produce small improvements in arterial saturation at the expense of systemic perfusion.

DiNardo JA. Transposition of the great vessels. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2005: 357–380.

B.3. What is the plan for glucose management in this patient?

Maintenance for caloric requirements in the awake neonate/infant are 100 kcal/kg/day or 4 kcal/kg/hour. This caloric requirement can be met with glucose 25 g/kg/day or 1 g/kg/hour. From a practical point of view, this glucose requirement can be met with 10% dextrose (100 mg/mL) run at the maintenance volume replacement rate of 4 mL/kg/hour. Ten percent dextrose run at half this rate (2 mL/kg/hour) is usually sufficient to meet the caloric requirements of an anesthetized infant while avoiding both the hyperglycemia and hypoglycemia that can be detrimental to neurologic outcome particularly following deep hypothermic circulatory arrest (DHCA). Dextrose infusions should be discontinued before commencement of CPB because the associated neuroendocrine response to CPB generally produces mild hyperglycemia. Some infants receive nutritional support as part of medical stabilization before surgery. High-calorie total parenteral nutrition and intralipid therapy should be discontinued and replaced with a 10% dextrose infusion several hours before transport to the OR. Continued administration of these high-calorie

infusions makes intraoperative serum glucose management problematic. In these patients, higher dextrose infusion rates may be necessary pre-CPB to avoid rebound hypoglycemia.

DiNardo JA. Anesthesia for congenital heart surgery. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart Disease*. London: Arnold; 2004:45–65.

C. Intraoperative Management

C.1. How would you monitor this infant?

Ideally, preinduction monitoring should include a blood pressure cuff, ECG, pulse oximeter, and an end-tidal carbon dioxide monitor. In reality, a pulse oximeter and an ECG may be all that is practical in the early stages of induction. The other monitors are then quickly added as induction progresses. Pulse oximeter probes should be placed on an upper and lower extremity (preductal and postductal if relevant). An intra-arterial catheter (radial or femoral) is placed just after induction. Many infants transferred from the ICU will have an umbilical artery or femoral artery catheter in place. A central venous pressure and drug infusion catheter is placed after intubation and stabilization. Double-lumen central venous catheters inserted through the femoral or internal jugular vein are preferred. Nasopharyngeal, tympanic, and rectal temperature probes are also placed following induction. A bladder catheter should be placed. A TEE probe can be inserted following induction and intubation.

DiNardo JA. Anesthesia for congenital heart surgery. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart Disease*. London: Arnold; 2004:45–65.

C.2. What would be the best method of induction?

This infant would have an IV catheter in place on transfer to the OR. Anesthesia is generally induced and maintained using a synthetic opioid-based (fentanyl or sufentanil) technique. These opioids may be used alone in high doses (25 to 100 μg/kg fentanyl or 2.5 to 10 μg/kg sufentanil) or in low to moderate doses (5 to 25 μg/kg fentanyl or 0.5 to 2.5 μg/kg sufentanil) in combination with an inhalation agent (generally isoflurane or sevoflurane) or a benzodiazepine (generally midazolam). The high-dose technique is particularly useful in neonates and infants. High-dose opioids provide hemodynamic stability, do not depress the myocardium, and blunt reactive pulmonary hypertension. In order to avoid bradycardia, pancuronium (0.1 mg/kg) is administered in conjunction with the opioid; its vagolytic activity offsets the vagotonic activity of the narcotics.

DiNardo JA. Anesthesia for congenital heart surgery. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart Disease*. London: Arnold; 2004:45–65.

DiNardo JA. Transposition of the great vessels. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2005: 357–380.

C.3. Is CPB in infants and children different from adults?

The major differences between adult and pediatric CPB are summarized in Table 39.2.

Table 39.2 Major Differences between Adult and Pediatric Cardiopulmonary Bypass

PARAMETER	ADULT	PEDIATRICS
Hypothermic temperature	Rarely below 25° C–32° C	Commonly 15° C–20° C
Use of total circulatory arrest	Rare	Common
Pump prime		
Dilution effects on blood volume	25%–33%	200%–300%
Additional additives in ped primes		Blood, albumin
Perfusion pressures	50–80 mm Hg (some centers accept 30 mm Hg)	20–50 mm Hg
Influence of pH management strategy	Minimal at moderate hypothermia	Marked at deep hypothemia
Measured $Paco_2$ differences	30–45 mm Hg	20–80 mm Hg
Glucose regulation		
Hypoglycemia	Rare—requires significant hepatic injury	Common—reduced hepatic glycogen stores
Hyperglycemia	Frequent—generally easily controlled with insulin	Less common—rebound hypoglycemia may occur

Flows of 2.0 to 2.5 L/minute/m^2 are commonly used for infants, children, and adults during mild to moderate systemic hypothermia. Owing to age-related differences in the relationship of surface area to weight, these flow rates expressed in mL/kg/minute will be substantially higher in the neonate than in the adult. The recommended full flow rates for pediatric CPB are summarized in Table 39.3.

The vast majority of operative procedures in children require the use of either total CPB or DHCA. Venous cannulation for DHCA is usually accomplished with a single large venous cannula in the RA. Once cooling is complete and circulatory

Table 39.3 Recommended Full Flow Rates for Pediatric Cardiopulmonary Bypass

PATIENT WEIGHT (kg)	FULL CPB FLOW RATES (mL/kg/min)
<3	150–200
3–10	125–175
10–15	120–150
15–30	100–120
30–50	75–100
>50	50–75

CPB, cardiopulmonary bypass.

arrest is established, the cannula is removed to allow for maximum exposure. For total CPB, once the cavae (and other sources of systemic venous return) are cannulated, surgical tourniquets or tapes are passed around the external circumference of the vessels. When these tapes are tightened around the cannulae, the right heart can be isolated completely and subsequently opened without entrainment of air into the venous circuit or obscuration of the surgical field by venous blood. During delivery of antegrade cardioplegia, it is essential that at least one tape be left untightened to allow egress of cardioplegia solution from the coronary sinus without distention of the RA. In older children, a larger cannula is used in the inferior vena cava (IVC) as compared with the superior vena cava (SVC), because a larger portion of systemic venous return (two-thirds) is from the IVC.

As with venous cannulation, arterial cannulation in children particularly infants/neonates can be technically challenging. It may be necessary in circumstances where the ascending aorta and aortic arch are hypoplastic and systemic blood flow is ductal dependent (as in hypoplastic left heart syndrome) to obtain systemic perfusion through the ductus arteriosus by cannulating the PA. When the aortic arch is interrupted, cannulation of the aorta both proximal and distal to the interruption is necessary. Because the arterial cannula is relatively large as compared to the aorta in infants/neonates, complete or partial obstruction of the aorta by the cannula itself is possible. Constant vigilance is necessary to avoid this problem. If dampening of the arterial trace, distension of the systemic ventricle, or an increase in CPB line pressure occurs with placement or manipulation of the arterial cannula, the surgeon should immediately be made aware of the situation so the cannula can be repositioned. Some centers utilize near-infrared spectroscopy and transcranial Doppler ultrasonographic technology as adjunctive methods to assess cerebral blood flow during CPB.

Davies LK. Cardiopulmonary bypass in infants and children: how is it different? *J Cardiothorac Vasc Anesth.* 1999;13(3):330–345.

DiNardo JA. Physiology and techniques of extracorporeal circulation in the pediatric patient. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia.* 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2005:228–252.

DiNardo JA. Profound hypothermia and circulatory arrest. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia.* 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2005:253–265.

C.4. What is modified ultrafiltration (MUF)?

Ultrafiltrators are devices commonly added to the CPB circuit to remove excess fluid and produce hemoconcentration. When used in conjunction with CPB, these devices produce an ultrafiltrate that occurs as the result of a hydrostatic pressure gradient across a semipermeable membrane. These are the same devices that can be used for hemodialysis when they are used in conjunction with a dialysate. When used in conjunction with CPB, they are commonly called *hemoconcentrators* because they produce an increase in hematocrit by removing excess fluid.

These devices consist of a core of microporous hollow fibers made of polysulfone, polyamide, or polyacrylonitrile material arranged in a bundle. The pore size is generally 0.30 to 0.40 μm. Owing to the pressure drop across the device, blood inflow must be obtained from the arterial side of the CPB circuit while blood outflow is diverted to the cardiotomy reservoir or venous reservoir. The ultrafiltrate is collected in a container connected to a vacuum source.

The ultrafiltrate is discarded and has the composition of glomerular filtrate. The rate at which ultrafiltrate is produced is dependent on the transmembrane pressure (TMP) gradient. TMP is determined by the arterial inlet pressure (P_a), the venous

outlet pressure (P_v), the absolute value of applied suction at the outlet (P_n), the oncotic pressure at the inlet (P_i), and the oncotic pressure at the outlet (P_o):

$$\text{TMP} = \frac{P_a + P_v}{2} + P_n - \frac{P_i + P_o}{2}$$

P_n is increased by using the regulated vacuum source connected to the outlet of the device. TMP should not exceed 500 mm Hg.

Continuous ultrafiltration (CUF) refers to ultrafiltration occurring throughout CPB or during those intervals when venous reservoir volume is sufficient to allow it. MUF is a technique that allows ultrafiltration to continue after weaning from CPB. MUF may be performed utilizing either an arteriovenous or venovenous system. In the arteriovenous system, inflow to the ultrafiltrator during MUF is directly from the aortic cannula. Outflow from the ultrafiltrator is to the RA. Blood volume is kept constant as ultrafiltrate is lost by replacing it with blood from the CPB circuit, which passes through the ultrafiltrator before being delivered to the RA. In this way, the CPB circuit can remain primed and the patient's blood, as well as the CPB blood, can be hemoconcentrated. In the venovenous system, the IVC cannula provides inflow to the ultrafiltrator with the aid of a roller pump, whereas outflow from the ultrafiltrator is returned to the SVC cannula. Blood volume is kept constant as ultrafiltrate is lost by replacing it with blood from the CPB circuit, which passes through the ultrafiltrator before being delivered to the SVC. The end point for termination of MUF following CPB varies from institution to institution, with institutions terminating MUF after a set time interval (15 to 20 minutes), a set hematocrit (40%), or a set volume removed (750 mL/m^2). Heparin anticoagulation must be maintained during MUF, with protamine reversal of heparin initiated after termination of MUF.

MUF may be an effective method of attenuating the deleterious consequences of a CPB strategy that involves large asanguinous primes, particularly in neonates and infants. In the studies comparing MUF to no ultrafiltration, a CPB technique consisting of a very large asanginous pump prime (400 to 900 mL) with packed cells added to reach a hematocrit of 15% to 20% has generally been used. This is precisely the group of patients who would need and who would benefit from aggressive removal of excess fluid to reduce total body water and increase hematocrit and coagulation factors. Furthermore, it has been demonstrated that MUF and continuous ultrafiltration during CPB are indistinguishable in their effect on hematocrit, mean arterial pressure, HR, and LV shortening fraction when equal volumes of fluid are removed.

DiNardo JA. Physiology and techniques of extracorporeal circulation in the pediatric patient. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2005:228–252.

Thompson LD, McElhinney DB, Findlay P, et al. A prospective randomized study comparing volume-standardized modified and conventional ultrafiltration in pediatric cardiac surgery. *J Thorac Cardiovasc Surg*. 2001;122:220–228.

C.5. Briefly describe the surgical techniques of the Mustard/Senning, ASO, and Rastelli procedures.

Intra-atrial physiologic repairs: Mustard and Senning procedures

In both procedures, the interatrial septum is excised, creating a large ASD. In the Mustard procedure, a baffle made of native pericardium or synthetic material is then used to redirect pulmonary and systemic venous blood. In the Senning procedure, autologous tissue from the right atrial wall and interatrial septum is used in place of the pericardium or synthetic material. In either case, pulmonary venous blood flows over the baffle and is directed across the tricuspid valve into the RV and out the aorta.

Systemic venous blood flows on the underside of the baffle to be directed across the mitral valve into the LV and out of the PA. This arrangement results in physiologic but not anatomic correction of D-TGA, as the morphologic RV becomes the systemic ventricle. These procedures are performed with hypothermic CPB, bicaval cannulation, and aortic cross clamping during cardioplegic arrest. Intervals of LFCPB are customarily used.

Arterial anatomic repair: arterial switch (Jatene) operation

The PA and the aorta are transected distal to their respective valves. The coronary arteries are initially explanted from the ascending aorta with 3 to 4 mm of surrounding tissue. The explant sites are repaired either with pericardium or synthetic material. The coronary arteries are reimplanted into the proximal PA (neoaorta). The distal PA is brought anterior to the aorta (LeCompte maneuver) to be reanastomosed to the old proximal aorta (right ventricular outflow) and the distal aorta reanastomosed to the old proximal PA (left ventricular outflow). As a result, the great arteries are switched to create ventriculoarterial concordance with both an anatomic and physiologic repair achieved. The ASO is done using hypothermic CPB with aortic cross clamping and cardioplegic arrest. Intervals of LFCPB are customarily used. A short interval of DHCA may be employed to close the atrial septum or VSD if a single venous cannula rather than bicaval venous cannulation is used. Closure of a VSD is preferentially done transatrially through the tricuspid valve. It is desirable to avoid approaching a VSD through the RV, because an incision in the RV may contribute substantially to postoperative RV dysfunction.

DiNardo JA. Transposition of the great arteries. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart Disease*. London: Arnold; 2004:256–278.

Jatene AD, Fontes VF, Paulista PP, et al. Anatomic correction of transposition of the great vessels. *J Thorac Cardiovasc Surg*. 1976;72:364–370.

Rastelli procedure

The PA is transected and ligated just distal to or at the level of the pulmonary valve. A right ventriculotomy is performed, and the VSD is closed with a patch tunnel such that the LV is in continuity with the aorta. The VSD may have to be enlarged, in some cases, to prevent subaortic stenosis. RV to PA continuity is achieved by placement of valved conduit or valved homograft between the right ventriculotomy site and the proximal main PA. The result is LV to aortic continuity and RV to PA continuity with bypass of the subpulmonic and pulmonic stenosis. This procedure is performed with hypothermic CPB, bicaval cannulation, and aortic cross clamping during cardioplegic arrest. Intervals of LFCPB are customarily used.

Historically, most of these patients had a palliative systemic to PA shunt placed in the newborn period and then returned for the Rastelli procedure and takedown of the shunt at 2 to 3 years of age. The delay was felt necessary to avoid performing a right ventriculotomy in infants with immature myocardium and limited contractile elements and to allow adequate growth of the RV and pulmonary arteries to permit placement of an RV to PA conduit. In the current era with improvements in myocardial protection, CPB technology, and surgical technique, this procedure can be performed as a primary procedure in the neonatal period.

DiNardo JA. Transposition of the great arteries. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart Disease*. London: Arnold; 2004:256–278.

DiNardo JA. Transposition of the great vessels. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2005:357–380.

C.6. What is hypothermia and how is it classified? What is low-flow cardiopulmonary bypass (LFCPB)? What is deep hypothermic circulatory arrest (DHCA)?

The levels of systemic hypothermia employed during CPB are generally defined as follows: mild (35° C [95° F] to 32° C [89.6° F]), moderate (31° C [87.8° F] to 26° C [78.8° F]), deep (25° C [77° F] to 20° C [68° F]), and profound (<20° C [68° F]). Unfortunately, it is not uncommon for temperatures less than 20° C (68° F) used in conjunction with pediatric cardiac surgery to be called *deep hypothermia*. Low-flow CPB in neonates/infants conducted in conjunction with temperatures of 18° C (64.4° F) to 25° C (77° F) is generally defined as 50 to 70 mL/kg/minute or approximately 1.0 to 1.5 L/minute/m^2.

Profound hypothermic circulatory arrest, commonly referred to as *DHCA*, is a technique employed to improve exposure of intracardiac defects and to facilitate aortic arch reconstruction in infants and children. DHCA is conducted in conjunction with temperatures of 18° C (64.4° F) to 20° C (68° F) and allows cessation of CPB, venous and arterial cannula removal, and exsanguination of the patient into the venous reservoir of the CPB circuit. There has been substantial refinement of the technique of DHCA since its successful inception in the 1970s. In the current era, DHCA is used selectively and for short intervals. It is utilized primarily for the aortic arch reconstruction component of the Norwood procedure, repair of interrupted aortic arch, neonatal repair of total anomalous pulmonary venous connection, and complicated intracardiac repairs such as complete AV canal defects in small (<2.0 kg) neonates and infants.

Davies LK. Cardiopulmonary bypass in infants and children: how is it different? *J Cardiothorac Vasc Anesth.* 1999;13(3):330–345.

DiNardo JA. Physiology and techniques of extracorporeal circulation in the pediatric patient. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia.* 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2005:228–252.

DiNardo JA. Profound hypothermia and circulatory arrest. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia.* 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2005:253–265.

C.7. Why is hypothermia beneficial to the brain during LFCPB and DHCA?

Hypothermia is arguably the most important component of LFCPB and DHCA. Hypothermia-induced reduction in cerebral metabolic rate for oxygen ($CMRO_2$) slows the rate of depletion of high-energy phosphates and the development of intracellular acidosis. This in turn delays or prevents the neuronal energy failure that leads to terminal membrane depolarization and subsequent neuronal injury or death during an ischemic episode. Q_{10} defines the ratio of organ O_2 consumption at a defined temperature to the O_2 consumption at a temperature 10° C (18° F) lower. The cerebral Q_{10} is approximately 3.65 in children and 2.3 in adults. Despite this, the cerebral metabolic rate will still be approximately 10% to 15% of its normothermic baseline at 15° C (59° F). If it is assumed that 3 to 5 minutes of cerebral ischemia can be tolerated at 37° C (98.6° F) and the Q_{10} is 3.0, 9 to 15 minutes of ischemia can be tolerated at 27° C (80.6° F) and 27 to 45 minutes can be tolerated at 17° C (62.6° F).

In addition to reducing $CMRO_2$, hypothermia also serves to ameliorate some of the sequalae of neuronal ischemia when instituted *before* the ischemia insult. Specifically, hypothermia markedly reduces release of the excitatory neurotransmitters glutamate, aspartate, and glycine that accompany cerebral ischemia and subsequent reperfusion. In energy-deprived cells, glutamate in particular is neurotoxic in part due to the role it plays in inducing massive calcium influx through N-methyl-D-aspartic acid receptors.

Hypothermia also blunts the inhibitory effect of hypoxia on nitroxidergic (postganglionic parasympathetic nerve where nitric oxide is the neurotransmitter)-induced cerebral vasodilatation. In addition, there is evidence that hypothermia may attenuate neutrophil migration into ischemic tissue.

DiNardo JA. Profound hypothermia and circulatory arrest. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2005:253–265.

McCullough JN, Zhang N, Reich DL, et al. Cerebral metabolic suppression during hypothermic circulatory arrest in humans. *Ann Thorac Surg*. 1999;67:1895–1899.

C.8. Explain the difference between α-stat and pH-stat blood gas management.

pH-stat and α-stat acid–base management are commonly discussed in association with management of CPB. pH-stat and α-stat regulation are acid–base management methods that directly influence blood flow to the brain and other organs. Although pH-stat and α-stat acid–base management are commonly mentioned in association with temperature-corrected and temperature-uncorrected blood gases, it must be emphasized that these are entirely different concepts. The method of blood gas interpretation (corrected or uncorrected) does not dictate the method of acid–base management (pH-stat or α-stat). α-stat or pH-stat management is possible with use of both temperature-corrected and temperature-uncorrected blood gases. In addition, it is important to point out that at a patient temperature of 37° C (98.6° F), there is no difference between pH-stat and α-stat management. The difference between these two strategies becomes more marked as patient temperature progressively decreases below 37° C (98.6° F) and is not clinically relevant until patient temperature is less than 30° C (86° F).

When a blood gas sample is drawn from a patient at 25° C (77° F) and sent to the blood gas laboratory, the sample is warmed to 37° C (98.6° F) before measurement. The values obtained at 37° C (98.6° F) are called the *temperature-uncorrected values*. These values are converted to temperature-corrected values using a nomogram. The nomogram accounts for temperature-induced changes in pH, O_2 solubility, and CO_2 solubility in a closed-blood system. When blood in a closed system is cooled to a lower temperature, the electrochemically neutral pH is higher and the associated P_{CO_2} is lower than in a closed blood system at 37° C (98.6° F). Therefore, electrochemical neutrality is maintained by keeping pH alkalotic in temperature-corrected blood gases and normal in temperature-uncorrected gases. This is known as *α-stat regulation*. For practical purposes, it is easier to use uncorrected gases and keep pH and P_{CO_2} in the range considered normal at 37° C (98.6° F). It has been demonstrated clinically that cerebral blood flow and oxygen consumption are appropriately coupled when α-stat regulation is used. Deep hypothermia in the presence of α-stat regulation produces loss of cerebral autoregulation such that cerebral blood flow varies directly with arterial pressure.

pH-stat regulation refers to maintaining pH and P_{CO_2} at normal values for blood at 37° C (98.6° F) regardless of actual blood temperature. With this strategy, a blood sample will have a normal pH and P_{CO_2} when temperature-corrected gases are used, and acidotic pH and P_{CO_2} values when temperature-uncorrected gases are used. For practical purposes, pH-stat is maintained by adding CO_2 to the ventilating gas during hypothermic CPB to increase P_{CO_2} and decrease the pH. In contrast to α-stat regulation, in which total CO_2 content is kept constant, pH-stat regulation results in an increase in total CO_2 content. The cerebral vasculature maintains vasomotor responses to varying P_{CO_2} during hypothermic CPB. This

response is maintained during both moderate and deep hypothermia despite the fact that deep hypothermia induces loss of cerebral blood flow autoregulation. It has been demonstrated clinically that when pH-stat regulation is used with moderate hypothermic CPB, there is uncoupling of cerebral blood flow and metabolism and loss of cerebral autoregulation. As a result, cerebral blood flow varies linearly with arterial blood pressure, and cerebral hyperperfusion exists with cerebral blood flow far in excess of that dictated by cerebral metabolic rate. This hyperperfusion state is the result of (1) reduced cerebral oxygen consumption induced by hypothermia and (2) cerebral vasodilation resulting from a disproportionately high P_{CO_2} for the degree of hypothermia present. The potential danger of the hyperperfused state is that it may result in increased delivery of microemboli into the cerebral circulation.

DiNardo JA. Physiology and techniques of extracorporeal circulation in the pediatric patient. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2005:228–252.

DiNardo JA. Profound hypothermia and circulatory arrest. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2005:253–265.

C.9. What are the immediate post-CPB issues following ASO?

Bleeding from the extensive suture lines in the post-CPB period may be problematic. Efforts to reduce aortic blood pressure combined with aggressive blood component therapy are often required. In neonates, it may require 1 to 2 units of platelets (0.25 to 0.5 units/kg) to obtain a therapeutic platelet count increase. Because platelets are suspended in fresh frozen plasma, a platelet transfusion of this size usually results in a fresh frozen plasma transfusion of 10 to 15 mL per kg.

Myocardial ischemia following reimplantation of the coronary arteries is a potential problem following the ASO. In some circumstances, the ischemia is transient secondary to coronary air emboli. TEE is very useful to ensure adequate removal of air from the LA and LV before the termination of CPB. It is also useful in assessing the potency of the reimplanted coronary arteries. Maintenance of high perfusion pressures on CPB after aortic cross clamp removal will facilitate the distal migration of air emboli. In other instances, kinking of the reimplanted artery or compromise of the implanted coronary ostia may require immediate surgical intervention. Pharmacologic intervention with traditional therapies to improve the balance of myocardial oxygen demand and delivery such as nitroglycerin and β-blockade are never a long-term alternative to prompt surgical revision of the appropriate anastomosis.

Despite comprehensive preoperative evaluation, the LV of patients undergoing an ASO may be marginal in its ability to support the systemic circulation in the post-CPB period. This may occur as the result of myocardial ischemia, inadequate LV mass, poor protection of the LV during aortic cross clamping, or a combination of these variables. TEE is useful in identifying and continuously evaluating both global and regional LV systolic dysfunction. It also detects mitral regurgitation, which may occur secondary to papillary muscle dysfunction or to dilation of the mitral valve annulus. Inotropic support of the LV and afterload reduction may be necessary to terminate CPB.

DiNardo JA. Transposition of the great vessels. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2005:357–380.

D. Postoperative Management

D.1. How is myocardial ischemia addressed in the intensive care unit (ICU) following the ASO?

Myocardial ischemia in the ICU following an ASO as heralded by ST-segment/T-wave changes or the development of atrial or ventricular arrhythmias requires immediate attention. Myocardial ischemia should be considered to be mechanical in nature until proved otherwise. Compression of the coronary ostia by swelling of thrombin gelform pads or thrombus formation around the coronary anastomoses must be considered. In this setting, surgical reexploration is likely to be immediately therapeutic.

Another source of mechanically induced myocardial ischemia in the ASO patient occurs as the result of LV dilation. A unique cycle of LV dilation initiating and exacerbating myocardial ischemia exists in patients having undergone the ASO. Myocardial ischemia, afterload mismatch, or overzealous volume infusion can result in LV distension and LA hypertension. This will be particularly likely if there is mitral insufficiency from either papillary muscle dysfunction or dilation of the mitral valve annulus. LV distension may result in tension on and kinking of the coronary reanastomosis sites. LA hypertension produces elevations in PA pressure and distension of the PA. As the LeCompte maneuver brings the distal PA anterior to the ascending aorta, distension of the PA may actually compress or place tension on the coronary ostia. The resulting myocardial ischemia produces further LV dilation, progressive elevations in LA and PA pressures, and continuing compromise of coronary blood flow. Attempts to induce coronary vasodilatation with nitroglycerine are unlikely to be beneficial in this setting, although its preload and afterload reducing may be beneficial. A more rational approach would be initiation of milrinone therapy.

DiNardo JA. Transposition of the great vessels. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2005:357–380.

DiNardo JA. Transposition of the great arteries. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart Disease*. London: Arnold; 2004:256–278.

D.2. What immediate postoperative problems would be anticipated following the Rastelli procedure?

Right (pulmonary) ventricular dysfunction may occur in the post-CPB period. These patients are at risk because a right ventriculotomy is used to close the VSD and to create the new pulmonary outflow tract. Heart block may also occur given the proximity of the VSD to the intraventricular conduction pathways. A residual VSD may be present. Because the VSD closure to create LV to aortic continuity is more of a tunnel than a patch closure, LV outflow tract obstruction is also possible.

DiNardo JA. Transposition of the great vessels. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2005: 357–380.

D.3. What intermediate and long-term surgical problems are seen after ASO?

Supravalvular pulmonary stenosis is probably the most common complication of ASO. This stenosis is due to retraction of the tissue used to replace the tissue excised with the explanted coronaries and, in most patients, is not extensive enough

to result in valvular pulmonary stenosis. Series with long-term follow-up (15 years) confirms that the incidence of supravalvular stenosis severe enough to require reoperation (generally a gradient >50 to 60 mm Hg) is approximately 4% to 8%. Aortic insufficiency occurs in approximately 10% to 15% of patients at long-term follow-up, with the majority (96%) graded as trivial or mild. Time has shown aortic insufficiency to be a rare source of morbidity or indication for reoperation following the ASO.

Early concerns existed regarding the long-term patency and growth potential of the reimplanted coronary arteries. Fortunately these problems have not materialized on a large scale.

DiNardo JA. Transposition of the great vessels. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2005: 357–380.

Legendre A, Losay J, Touchot-Kone A, et al. Coronary events after arterial switch operation for transposition of the great arteries. *Circulation*. 2003;108(suppl 1): II186–II190.

Nogi S, McCrindle BW, Boutin C, et al. Fate of the neopulmonary valve after the arterial switch operation in neonates. *J Thorac Cardiovasc Surg*. 1998;115:557–562.

D.4. What are the long-term outcomes after ASO?

The initial result for the arterial switch in experienced institutions is excellent, with an actuarial survival at 1 year of 90% for patients with D-TGA and IVS, and 83% for patients with D-TGA and VSD. Other experienced groups have reported similar results. A recent review of 470 patients from one institution experienced in the ASO, however, revealed a 1-year survival rate of 92% and an 8-year survival rate of 91% for patients with both D-TGA and IVS and D-TGA and VSD. A similar review of 1,200 patients from another experienced institution revealed a 1- and 15-year survival rate of 92% for patients with D-TGA and IVS, and 1- and 15-year survival of 81% and 80% for D-TGA and VSD, respectively. A recent multi-institution review of 631 patients with D-TGA and 167 patients with D-TGA and VSD reviewed similar initial and long-term (15 years) outcomes.

The overwhelming majority (90% to 97%) of patients have normal-sized, patent coronary arteries as assessed by coronary angiography. A recent study of a large cohort demonstrated that survival without coronary events (death from myocardial infarction, sudden death, and reoperation for coronary stenoses) is 92.7% at 1 year and 88.2% at 15 years. The incidence of coronary events is bimodal with a high early and low late event rate. Eighty-nine percent of all coronary events occurred in the first 3 months after ASO. The event rate did not increase again until 6 years after ASO. Two types of coronary anatomy (a single coronary artery origin or two coronaries originating close to each other at a facing commissure) were risk factors for a coronary event.

One of the potential advantages of the ASO over the atrial switch procedure is the use of the native LV as the systemic ventricle. Long-term follow-up indicates that patients who have undergone an ASO have higher systemic ventricular ejection fractions than do patients who have undergone atrial switch procedures. In fact, patients who had D-TGA and IVS repaired in infancy and patients who had D-TGA and VSD repaired later have LV end diastolic dimensions and contractile indices similar to normal patients. Myocardial contractility in patients having undergone a rapid or traditional two-stage arterial switch is mildly depressed as compared to patients having undergone a primary arterial switch. No progression of this ventricular dysfunction has been noted at either intermediate or long-term follow-up.

DiNardo JA. Transposition of the great vessels. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2005: 357–380.

Losay J, Touchota A, Serraf A, et al. Late outcome after arterial switch operation for transposition of the great arteries. *Circulation*. 2001;104:I121–I126.

Pasquali SK, Hasselblad V, Li JS, et al. Coronary artery pattern and outcome of arterial switch operation for transposition of the great arteries: a meta-analysis. *Circulation*. 2002;106:2575–2580.

Wernovsky G, Mayer JE Jr, Jonas RA, et al. Factors influencing early and late outcome of the arterial switch operation for transposition of the great arteries. *J Thorac Cardiovasc Surg*. 1995;109:289–301; discussion 301–302.

Williams WG, McCrindle BW, Ashburn DA, et al. Outcomes of 829 neonates with complete transposition of the great arteries 12–17 years after repair. *Eur J Cardiothorac Surg*. 2003;24:1–10.

D.5. What are the long-term outcomes after Rastelli repair for D-TGA with left ventricular outflow tract (LVOT) obstruction?

Outcome following the Rastelli procedure for TGV with VSD and LVOT obstruction is good, with a near 100% early survival rate. One large recent series reports freedom from death or transplantation to be 82% at 5 years, with a progressive decrease to 52% by 20 years. Similar results are reported in another recent series. The need for reintervention (either surgical or catheterization) increases over time. Intervention to relieve RVOT (RV to PA conduit) obstruction accounts for 75% of all interventions, with pacemaker insertion and relief of LVOT obstruction (aortic outflow) accounting for most of the remaining interventions. Freedom from surgical or catheterization intervention for relief of conduit obstruction is 56% at 5 years, decreasing to 21% at 15 years. Patients who had undergone the Rastelli procedure were reported to have increased LV end-diastolic and end-systolic volumes and diminished LV contractile function compared with normal subjects. Despite this, the majority (98%) of these patients were found to be in New York Heart Association functional class 1 or 2 following the Rastelli procedure. It is unclear whether surgery at an earlier age and improvements in construction of the VSD tunnel patch has reduced the incidence of contractile dysfunction following the Rastelli procedure in the current era.

Dearani JA, Danielson DK, Puga FJ, et al. Late follow-up of 1095 patients undergoing operation for complex congenital heart disease utilizing pulmonary ventricle to pulmonary artery conduits. *Ann Thorac Surg*. 2003;75:399–410.

D.6. What is long-term neurologic outcome like after ASO?

The best assessment of neurologic outcome following ASO is data from the Boston Circulatory Arrest Trial. In this trial, infants undergoing ASO for D-TGA with IVS or VSD randomized 171 infants to a strategy of either DHCA or LFCPB using α-stat pH management. Infants in the DHCA group underwent an average of 52 minutes of DHCA, whereas those in the LFCPB group underwent 14 minutes of DHCA.

At age 8 years, parents of children in the trial reported more problems with attention, learning, speech, and the frequency of developmental delay than parents of children in a normative sample. Despite this, children in the cohort had overall physical and psychosocial health status similar to the general population. Furthermore, there was no association between physical and psychosocial scores and the presence or

absence of a VSD or the use of LFCPB versus DHCA. Neurodevelopmental outcome in this cohort was generally not adversely affected unless the duration of DHCA exceeded 41 minutes. Beyond 41 minutes, there was a nonlinear (steadily worsening) outcome with increasing duration of DHCA.

Eight-year data from the trial also demonstrated that neurologic status, IQ, academic achievement, memory, problem solving, and visual–motor integration did not differ between the DHCA and LFCPB groups. Nonetheless, DHCA was associated with greater functional deficiencies (motor function, speech apraxia, visual–motor tracking, phonic awareness) than LFCPB (impulsive behavior, worse behavior as rated by teachers).

Bellinger DC, Wypij D, duPlessis AJ, et al. Neurodevelopmental status at eight years in children with dextro-transposition of the great arteries: the Boston Circulatory Arrest Trial. *J Thorac Cardiovasc Surg*. 2003;126:1385–1396.

DiNardo JA. Transposition of the great vessels. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2005:357–380.

Dunbar-Masterson C, Wypij D, Bellinger DC, et al. General health status of children with D-transposition of the great arteries after the arterial switch operation. *Circulation*. 2001;104:I138–I142.

Wypij D, Newburger JW, Rappaport LA, et al. The effect of duration of deep hypothermic circulatory arrest in infant heart surgery on late neurodevelopment: the Boston Circulatory Arrest Trial. *J Thorac Cardiovasc Surg*. 2003;126:1397–1403.

CHAPTER 40

Pyloric Stenosis

AARTI SHARMA AND VINOD MALHOTRA

A 3-WEEK-OLD FIRST-BORN MALE INFANT had projectile vomiting, which contained the ingested formula but no bile. His body weight is 2.5 kg. Serum electrolytes: K^+ 2.2 mEq per L, Cl^- 86 mEq per L. Blood pH 7.68. This infant was also noted to have a systolic murmur heard best at the second intercostal space along the left sternal border, which was assessed by a cardiologist and diagnosed as a ventricular septal defect (VSD).

A. Medical Disease and Differential Diagnosis

1. What is the diagnosis in this patient?
2. What is the differential diagnosis of pyloric stenosis?
3. What are the metabolic problems in this newborn secondary to his disease?
4. What are the adverse effects of metabolic alkalosis?
5. How would you treat this infant?
6. How would you determine fluid replacement in a newborn, and what fluids would you use?
7. How would you correct the metabolic alkalosis in this patient?
8. What causes a cardiac murmur?

B. Preoperative Evaluation and Preparation

1. How would you evaluate this patient preoperatively?
2. How would you evaluate a heart murmur?
3. How would you differentiate between functional versus organic murmur?
4. What are the types of VSD? What type of shunt do they cause?
5. What are the risks of surgery and anesthesia in a patient with VSD?
6. How would you prepare this patient rapidly for emergency surgery? Is surgical intervention an acute emergency in this case?
7. How would you prepare this patient for anesthesia?

C. Intraoperative Management

1. What induction–intubation sequence would you use?
2. What are the anatomic characteristics of the airway in the newborn, and how do they differ from those in the adult?
3. How do you determine the size of an endotracheal tube in a pediatric patient?
4. What anesthesia system would you use and why?
5. What are the advantages and disadvantages of commonly employed nonrebreathing systems?
6. How would you monitor this patient intraoperatively?
7. How does the pulse oximeter function?
8. What factors affect the measurement of oxygen saturation by the pulse oximeter?

D. Postoperative Management

1. What are the complications that can occur in the postanesthesia recovery period?
2. How would you treat postextubation "croup" in this infant?

A. Medical Disease and Differential Diagnosis

A.1. What is the diagnosis in this patient?

The most likely diagnosis in this patient is pyloric stenosis. The factors that favor the diagnosis are as follows:

- Age—3 weeks (average age at onset; range 5 days to 5 months)
- Boy child (boy-to-girl ratio = 4:1)
- Projectile vomiting (characteristic)
- Contents—ingested formula, no bile

The resultant biochemical abnormality in this patient is a hypokalemic, hypochloremic, metabolic alkalosis.

Pyloric stenosis occurs in 3 of 1,000 infants born in the United States; its incidence may be increasing. It is more common in whites of Northern European ancestry, less common in blacks, and rare in Asians. Reduced nitric oxide in pyloric tissue may contribute to the pathogenesis of pyloric stenosis.

Behrman RE, Kleigman RM, Jenson HB, et al., eds. *Nelson Textbook of Pediatrics.* 18th ed. Philadelphia: WB Saunders; 2007:1557–1559.

A.2. What is the differential diagnosis of pyloric stenosis?

Pyloric stenosis is distinguished from other congenital anomalies that cause obstruction of the alimentary tract in the newborn. These other anomalies include chalasia of the esophagus, hiatus hernia, duodenal atresia, jejunal atresia, ileal atresia, pancreatic annulus, malrotation of the gut, intra-abdominal hernias, and Meckel's diverticulum. Pathognomonic features of pyloric stenosis include absence of bile staining of the vomitus and visible gastric peristaltic waves on abdominal examination along with the palpable pyloric mass. The diagnosis is commonly made clinically. An "olive" is sometimes palpated in the epigastrium just to the right of the midline. Diagnosis can be confirmed by abdominal ultrasound. Occasionally, an upper gastrointestinal series with barium may be necessary.

Behrman RE, Kleigman RM, Jenson HB, et al., eds. *Nelson Textbook of Pediatrics.* 18th ed. Philadelphia: WB Saunders; 2007:1557–1559.

A.3. What are the metabolic problems in this newborn secondary to his disease?

Metabolic changes occur secondary to protracted vomiting and comprise the characteristic hypokalemic, hypochloremic alkalosis, as evident in this infant. Hyponatremia, although present, may not be manifested in serum value determinations because of severe dehydration. Compensatory respiratory acidosis is a frequent finding; it results from hypoventilation that may be marked and associated with periods of apnea. In severe dehydration leading to circulatory shock, the lack of adequate perfusion coupled with impaired renal and hepatic function may produce an entirely different picture of metabolic acidosis with hyperventilation, resulting in respiratory alkalosis. Therefore, depending on the severity and duration of vomiting and the type of fluid replenishment, one can encounter wide variation in findings on arterial blood gas and electrolyte determinations. However, most frequent findings are hypokalemia, hyponatremia, hypochloremia, and primary metabolic alkalosis with secondary respiratory acidosis. The renal response to vomiting is twofold: serum pH initially is maintained by excretion of alkaline urine with sodium and potassium loss; with depletion of these electrolytes, the kidneys secrete acidic urine (paradoxic acidosis), further increasing the metabolic alkalosis. These findings are summarized in Table 40.1.

Behrman RE, Kleigman RM, Jenson HB, et al., eds. *Nelson Textbook of Pediatrics.* 18th ed. Philadelphia: WB Saunders; 2007:1557–1559.

Coté CJ, Todres ID, Goudsouzian NG, et al., eds. *A Practice of Anesthesia for Infants and Children.* 3rd ed. WB Saunders; 2001:306–307.

Davis PJ, Cladis FP, Motoyama EK, eds. Clinical management of specialized surgical problem. In: *Smith's Anesthesia for Infants and Children.* 8th ed. Philadelphia: Mosby; 2011:750–751.

A.4. What are the adverse effects of metabolic alkalosis?

- An increase in pH results in shifting of the oxygen-dissociation curve to the left, thereby binding more oxygen to the hemoglobin and unloading less oxygen at the tissue level. This phenomenon assumes even more importance in newborns because at 3 weeks they still have up to 70% fetal hemoglobin with an already low value of P50 (i.e., 20 to 22 mm Hg).
- Respiratory compensation is affected by hypoventilation with increased potential for atelectasis, as well as periods of apnea.

Table 40.1 Metabolic Findings in the Newborn Secondary to Pyloric Stenosis

SEVERITY OF DEHYDRATION	ARTERIAL BLOOD GASES				SERUM ELECTROLYTES			
	pH	Pco_2	CO_2	Po_2	NA	K	CL	HCO_3
Mild	↑	↑	↑	↔	↓↔	↓	↓↓	↑
Moderate	↑↑	↑↑	↑↑	↔	↓	↓↓	↓↓↓	↑↑
Severe	↓↓	↓	↓↓	↓	↓	↓↓	↓↓↓	↓↓

(↔), no change; ↑/↓, slight change; ↑↑/↓↓, moderate change; ↑↑↑/↓↓↓, marked change.

- Decrease in ionized calcium.
- Increased potential for seizures.

Behrman RE, Kleigman RM, Jenson HB, et al., eds. *Nelson Textbook of Pediatrics.* 18th ed. Philadelphia: WB Saunders; 2007:1557–1559.

A.5. How would you treat this infant?

Medical management of infant with pyloric stenosis is of acute urgency and should be taken early and vigorously. The principles of management can be grouped under the following three categories: supportive therapy, to stabilize the patient; diagnostic tests, to confirm the diagnosis and to monitor therapy; and surgery as the corrective therapy.

Supportive therapy

- Circulatory support
- Correction of electrolyte imbalance
- Prevention of aspiration

Fluids

The infant with pyloric stenosis is hypovolemic and dehydrated secondary to persistent vomiting. Dehydration severity can vary from mild hypovolemia to circulatory shock. The following parameters are good indicators of dehydration severity:

- Physical appearance—skin turgor, parched mucous membranes, sunken fontanels, sunken eyeballs
- Blood pressure—decreased
- Pulse—increased
- Urine output—decreased
- Weight (birth and present) and weight loss

Quantitative assessment of these parameters gives a fair estimate of the amount of total body fluid depletion. A wide-bore intravenous cannula should be placed and an infusion started immediately to correct the deficits and provide maintenance fluids.

Electrolytes

The patient is alkalotic, hypokalemic, hypochloremic, and hyponatremic and must be provided with necessary ions to replenish the deficit. Albumin or Ringer's lactate may be used to treat the shock first. Next, the deficit should be corrected; 0.45% to 0.9% saline in 5% to 10% dextrose. Potassium (usually 40 mEq per L) must be added to this to correct hypokalemia and aid in the correction of alkalosis. However, potassium infusion should be withheld until satisfactory renal function is established. Fluid therapy should be continued until the infant is rehydrated and serum bicarbonate concentration is <30 mEq per dL, which implies that the alkalosis has been corrected.

Prevention of aspiration

A nasogastric tube should be inserted to thoroughly empty the stomach, and the upper airway reflexes should be preserved.

Diagnostic tests

- To assess the severity of fluid and electrolyte derangement and to monitor therapy, the following should be evaluated: complete blood count, serum electrolytes, blood gases, blood urea nitrogen, electrocardiogram (for marked hypokalemia)
- To confirm the diagnosis—barium swallow, ultrasound imaging

Surgery

Pyloromyotomy is the definitive treatment for these infants. Ramstedt pyloromyotomy through a right upper quadrant transverse incision has been the traditional treatment for hypertrophic pyloric stenosis. Recently, laparoscopic and circumumbilical approaches have been introduced as alternative methods to improve cosmesis, but concerns about greater operative times, costs, and complications remain. Surgery should be carried out early, but only after the patient has been stabilized satisfactorily.

Behrman RE, Kleigman RM, Jenson HB, et al., eds. *Nelson Textbook of Pediatrics*. 18th ed. Philadelphia: WB Saunders; 2007:1557–1559.

Blatnik JA, Ponsky TA. Advances in minimally invasive surgery in pediatrics. *Curr Gastroenterol Rep*. 2010;12(3):211–214.

A.6. How would you determine fluid replacement in a newborn, and what fluids would you use?

The general principles of fluid therapy are based on fluid maintenance, correction of deficits, and replacement of losses.

Maintenance fluids

In the newborn maintenance fluids are as follows:

- First 48 hours of life—75 mL/kg/day or 3 mL/kg/hour
- 2 days to 1 month—150 mL/kg/day or 6 mL/kg/hour
- 1 month onward (up to 10 kg)—100 mL/kg/day or 4 mL/kg/hour

Estimation of the degree of dehydration in a newborn is shown in Table 40.2.

The maintenance fluids take into account the fluid losses occurring normally through the kidney, bowel, skin, and lungs. At birth, the kidney is still undergoing maturation and what may be called "a glomerular imbalance" exists. What it implies is that some mature glomeruli may be connected to the immature tubules and vice versa. Hence, the kidney is functionally limited at birth but undergoes rapid maturation during the first week of life.

Electrolytes

The newborn is an obligate sodium loser as well as a poor tolerator of excessive sodium overload. The maintenance electrolytes are as follows:

- Sodium—3 to 5 mEq/kg/day
- Potassium—2 to 3 mEq/kg/day
- Chloride—1 to 3 mEq/kg/day

Table 40.2 Estimation of the Degree of Dehydration in a Newborn

	MILD	MODERATE	SEVERE
Percent fluid loss	5	10	15–20
Skin turgor	Poor	Very poor	Parched
Mucous membrane and tongue	Dry	Dry	Parched
Fontanelle and eyes	normal	Sunken fontanelle	Sunken eyes
Urine	Concentrated oliguria	Oliguria	Oliguria, anuria
Pulse	Normal	Tachycardia	Marked tachycardia
Blood pressure	Normal	Hypotension	Marked hypotension, shock

Correction of deficits

Deficits take into account the previous unreplaced losses because of a period of no intake by mouth and dehydration resulting from increased losses (e.g., from vomiting, diarrhea, and increased body temperature). The amount of deficit can be assessed by physical examination (see Table 40.2), body weight loss, and hematocrit.

Replacement of losses

Replacing losses covers ongoing abnormal losses not covered by maintenance fluids. Intraoperatively, it covers evaporative losses from the operative site, third spacing, and losses from the lungs if dry gases are used in nonrebreathing circuits (Table 40.3).

The younger and more physically immature the patient, the higher skin permeability, the ratio of body surface area to weight and the metabolic demand. In addition, the use of radiant warmers and phototherapy increases insensible water loss.

Miller RD, ed. *Miller's Anesthesia.* 7th ed. Philadelphia: Churchill Livingstone; 2010:2559–2597.

A.7. How would you correct the metabolic alkalosis in this patient?

To correct the metabolic alkalosis in this patient, the underlying electrolyte derangements (hyponatremia, hypokalemia, and hypochloremia) must be corrected. We correct the deficits by using calculated volumes of 5% dextrose in normal saline or Ringer's lactate solution, which helps to restore sodium and chloride mainly. Dextrose, 5% with one-fourth strength normal saline, may be used to provide maintenance fluids. Once renal function is established, potassium supplements are added to the infusion. Depending on the deficit, this therapy can require anywhere from 12 to 72 hours. In severely alkalotic patients, HCl and NH_4Cl have been used to correct the derangement. However, we have rarely found it necessary.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia.* 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1193–1205.

A.8. What causes a cardiac murmur?

Cardiac murmurs are caused by turbulent blood flow across cardiac valves or septal defects and are audible sound waves in the range of 20 to 2,000 Hz. Most murmurs in pediatric patients are normal or innocent, occurring in almost 50% of all school-aged children but must be distinguished from those murmurs associated with significant structural heart disease. Auscultation is critically important in diagnosing these murmurs; however, echocardiography remains the gold standard.

Table 40.3 Fluid Requirement to Replace Intraoperative Fluid Losses (Except Blood Loss) in the Newborn

	FLUID REPLACEMENT (mL/kg/hr)
Minor surgery (e.g., herniorrhaphy)	1–3
Moderate surgery (e.g., pyloromyotomy)	3–5
Major surgery (e.g., intestinal)	5–7
Respiratory water loss due to dry gases	2

Allen HD, Driscoll DJ, Shaddy RE, et al. *Moss and Adams' Heart Disease in Infants, Children, and Adolescents*. 7th ed. Philadelphia: Lippincott Williams & Wilkins; 2008:58–65.

Pelech AN. The cardiac murmur. When to refer? *Pediatr Clin North Am*. 1998;45:107–122.

B. Preoperative Evaluation and Preparation

B.1. How would you evaluate this patient preoperatively?

The following information is necessary in evaluating this patient:

History

Onset of illness, frequency and amount of vomiting, last feeding, diarrhea, urine output, activity of the newborn (active or lethargic), and birth weight.

Physical examination

Present body weight (to determine the weight loss), temperature, signs of dehydration (skin turgor, mucous membranes, fontanels, eyeballs, blood pressure, pulse, color, and volume of urine), muscle tone, and level of consciousness.

Laboratory findings

Complete blood count, electrolytes, blood urea nitrogen and blood sugar, urinalysis, and arterial blood gases.

Based on the data available, we can determine the fluid and electrolyte status of the patient and correct these accordingly to stabilize for surgery and anesthesia.

B.2. How would you evaluate a heart murmur?

Heart murmurs can be innocent or organic. By definition, innocent murmurs occur in the absence of structural or physiologic cardiac disease. The clinical diagnosis of a normal or innocent murmur should occur in the setting of an otherwise normal history, physical examination, and appearance. The presence of a family history of hypertrophic cardiomyopathy; congenital cardiac disease; or unexplained infant, childhood, or early adult death is particularly worrisome. Perinatal history of prematurity, maternal diabetes, drug or toxin ingestion, fetal distress, and clearly definable chromosomal disorders have particular cardiorespiratory relevance. The initial approach to the evaluation of the cardiovascular system should include an assessment of the cardiorespiratory system functionality as a pump and delivery system. An index of exercise or play capacity should be sought as a component of assessing growth and development. The author would ask about exercise tolerance, shortness of breath, cyanotic episodes, growth (because congestive heart failure may manifest as failure to thrive), and symptoms of congestive heart failure.

Allen HD, Driscoll DJ, Shaddy RE, et al. *Moss and Adams' Heart Disease in Infants, Children, and Adolescents*. 7th ed. Philadelphia: Lippincott Williams & Wilkins; 2008:58–65.

B.3. How would you differentiate between functional versus organic murmur?

Normal murmurs of childhood are comprised of five systolic and two continuous types but never solely diastolic (Table 40.4). A functional murmur is usually soft, 1/6 or 2/6, and never associated with palpable thrill. Pathologic murmurs are usually louder, 3/6 or greater and are associated with other cardiovascular pathologic features.

Table 40.4 Innocent Murmurs of Childhood

SYSTOLIC MURMURS	CONTINUOUS MURMURS
Vibratory Still's murmur	Venous hum
Pulmonary flow murmur	Mammary arterial souffle
Peripheral pulmonary artery stenosis murmur	
Supraclavicular systolic murmur	
Aortic systolic murmur	

Allen HD, Driscoll DJ, Shaddy RE, et al. *Moss and Adams' Heart Disease in Infants, Children, and Adolescents*. 7th ed. Philadelphia: Lippincott Williams & Wilkins; 2008:58–65.

B.4. What are the types of VSD? What type of shunt do they cause?

One common classification of VSD is based on anatomic location.

- Type I defects, or supracristal defects (5% of all VSDs), are outflow defects located above the crista supraventricularis just under the annulus of aorta.
- Type II defects, or infracristal defects (80% of all VSDs), are lower in membranous septum beneath the crista supraventricularis.
- Type III defects, or canal type (11% incidence), are inlet VSDs that accompany complete atrioventricular canal. They result from partial failure of the endocardial cushions to fuse.
- Type IV, or muscular, defects (2% to 7% incidence), probably results from excessive resorption of septal tissue during the muscular septal formation. They may be located anywhere in the muscular septum and may be multiple (also known as the swiss cheese defect).

VSD is left-to-right shunt. Pathophysiologic effects of VSD include left-to-right shunting, pulmonary hypertension, and heart failure resulting from volume overload.

Allen HD, Driscoll DJ, Shaddy RE, et al. *Moss and Adams' Heart Disease in Infants, Children, and Adolescents*. 7th ed. Philadelphia: Lippincott Williams & Wilkins; 2008: 667–675.

B.5. What are the risks of surgery and anesthesia in a patient with VSD?

Infective endocarditis is a complication of most congenital cardiac anomalies, so the patient requires antibiotic prophylaxis. There is also risk of increasing the flow in the shunt or reversing the flow in the shunt, resulting from acute and persistent increases in systemic vascular resistance or decreases in pulmonary vascular resistance causing hypoxemia and congestive heart failure. Right ventricular infundibular hypertrophy may be present in the patients with a VSD. Normally, this is a beneficial change, because it increases the resistance to right ventricular ejection, leading to decrease in magnitude of the left-to-right shunt. Nevertheless, perioperative events that exaggerate this obstruction to right ventricular outflow, such as increased myocardial contractility or hypovolemia, must be minimized. Therefore, these patients are often

anesthetized with a volatile anesthetic. In addition, intravascular fluid volume should be maintained by prompt replacement of blood loss. During the anesthetic, a normal end-tidal carbon dioxide should be maintained and routine air bubble precautions should be taken.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone; 2008.

B.6. How would you prepare this patient rapidly for emergency surgery? Is surgical intervention an acute emergency in this case?

Hypertrophic pyloric stenosis is a medical emergency and not a surgical emergency. Therefore, no newborn should be subjected to the additional hazards of anesthesia and surgery until stabilized medically.

Behrman RE, Kleigman RM, Jenson HB, et al., eds. *Nelson Textbook of Pediatrics*. 18th ed. Philadelphia: WB Saunders; 2007:1557–1559.

B.7. How would you prepare this patient for anesthesia?

Fluid and electrolyte replacement should be accomplished satisfactorily; this may take anywhere from 12 to 72 hours depending on the patient's status. The next step is to empty the stomach through a wide-bore nasogastric tube, lavaging out the gastric contents and any leftover barium. Alternatively, an oral-gastric approach allows for passage of a tube with wider lumen that ensures better stomach emptying. Premedication is usually atropine (0.01 to 0.02 mg per kg) intravenous or intramuscular if the patient does not have intravenous line.

Davis PJ, Cladis FP, Motoyama EK, eds. Clinical management of specialized surgical problem. In: *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia: Mosby; 2011:750–751.

Gregory GA, ed. *Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 2002:101, 579–580.

C. Intraoperative Management

C.1. What induction–intubation sequence would you use?

These children should arrive to the operating room with an intravenous access. Standard monitors are placed. The stomach is emptied by inserting an orogastric tube after (atropine may be used as premedication). Because the stomach may not be completely emptied, a rapid-sequence induction and intubation with cricoid pressure is highly recommended. Nevertheless, a recent survey of anesthetists in the United Kingdom revealed that 66% of all inductions were performed intravenously with only 56% of cases applying cricoid pressure. There is also some controversy regarding the appropriateness of awake intubations in this situation. A recent study comparing awake, rapid-sequence, or modified rapid-sequence induction demonstrated faster and more successful tracheal intubations in babies whose vocal cords were paralyzed using cisatracurium (0.4 to 0.5 mg per kg), vecuronium (0.1 to 0.2 mg per kg), or rocuronium (0.6 to 1 mg per kg).

The patient can be induced with a mixture of 50% O_2 and 50% N_2O and sevoflurane or halothane, with spontaneous ventilation and gentle assist through the cricoid pressure

as respiration is depressed. The trachea is intubated with muscle relaxant but can be intubated without muscle relaxant if sufficient deeper planes of anesthesia are achieved. Awake intubation may be accomplished in skillful hands in a lethargic neonate or in a critically sick infant. In most cases, however, neonates presenting for this procedure are fit and do not require awake intubation, which can be more traumatic.

Davis PJ, Cladis FP, Motoyama EK, eds. Clinical management of specialized surgical problem. In: *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia: Mosby; 2011:750–751.

Zelicof-Paul A, Smith-Lockridge A, Schnadower D, et al. Controversies in rapid sequence intubation in children. *Current Opin Pediatr*. 2005;17:355–362.

Zöhr M. Anesthesia for the child with full stomach. *Current Opin in Anesthesiology*. 2007; 20(3):201–203.

C.2. What are the anatomic characteristics of the airway in the newborn, and how do they differ from those in the adult?

The special characteristics of the upper airway in the newborn are as follows:

- Nasopharynx—narrow nasal passages, obligate nasal breathers
- Oropharynx—large tongue, long and pendulous epiglottis
- Larynx—the distinctive features shown in Table 40.5

It is apparent, therefore, that the newborn who has low respiratory reserve can develop airway obstruction easily. The infant may present problems during intubation and tolerate airway trauma poorly.

Comparative anatomy of the larynx and trachea in the newborn and the adult is shown in Table 40.5.

Davis PJ, Cladis FP, Motoyama EK, eds. Induction, maintenance, and recovery. In: *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia: Mosby; 2011:365–394.

C.3. How do you determine the size of an endotracheal tube in a pediatric patient?

The two parameters of endotracheal tube sizes are the tube length and diameter, depending on the age of the child, as shown in Table 40.6. However, these are approximate sizes and one must have one size bigger and one size smaller tube available when selecting

Table 40.5 Comparative Anatomy of the Larynx and Trachea in the Newborn and the Adult

ANATOMIC FEATURES	NEWBORN	ADULT
Size	4 cm	10–13 cm
Shape	Funnel	Cylindrical
Position of the glottis	C3–4	C6
Narrowest point	1 cm below vocal cords	At vocal cords
Vocal cords	Slanting anteriorly	Transverse or slightly slanting posteriorly
Mucous membrane	Loose (swells easily)	More firmly bound

Table 40.6 Endotracheal Tube Size for Pediatric Patient

AGE	LENGTH	INTERNAL DIAMETER (MM)	FRENCH SIZES
Newborn	10	3.0	14
6 mo	12	3.5	16
1 y	14	4.0	18
2 y	15	4.5	20
4 y	16	5.0	22
6 y	17	5.5	24
8 y	18	6.0	26
10 y	19	6.5	28
12 y	20	7.0	30

any tube size. A simple way to remember these numbers is to know the sizes at newborn, 6 months, and 1 year. Between 2 and 12 years the following guide may be used:

- Tube length from tip to incisor teeth (cm) = 11 + age in years
- Tube internal diameter (mm) = 4 + age/4
  French size (French) = 18 + age
  External circumference (French) = ID (mm) × 4 + 2
  (French size means external circumference in millimeters, which equals π times external diameter; π = 3.1416)

Davis PJ, Cladis FP, Motoyama EK, eds. Induction, maintenance, and recovery. In: *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia: Mosby; 2011:365–394.

C.4. What anesthesia system would you use and why?

We employ the circle system with alight circuit. The circle system is more advantageous because it maintains heat and humidification better and offers the freedom of choosing varying gas flows. The controversy about the increased resistance in adult system is discounted by the fact that the respiration is assisted or controlled intraoperatively. Newer anesthesia machines use valves with much less resistance than older models. Dead space in these systems is no more than that of the Mapleson circuits.

Dorsch JA, Dorsch SE. *Dorsch & Dorsch Understanding Anesthesia Equipment*. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2008:209–218.

C.5. What are the advantages and disadvantages of commonly employed nonrebreathing systems?

Commonly used nonrebreathing systems include Bain Breathing circuit (Mapleson D system) and Jackson-Rees modification of Ayre's T-piece. They offer the following advantages and disadvantages:

Advantages

- Minimal dead space
- No valves, low resistance
- Lightweight

- Reservoir bag to assist ventilation
- Good appreciation of patient's respiratory exchange

Disadvantages

- High flow of fresh gases required
- Low flows may allow rebreathing of gases without CO_2 absorption
- Loss of heat and humidity because of high flow of cold, dry gases (Bain's circuit allows some heating of inspired gases by surrounding fresh gas flow tubing with expired gas tubing)
- Scavenging problems of waste gases

Dorsch JA, Dorsch SE. *Dorsch & Dorsch Understanding Anesthesia Equipment*. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2008:191–208.

C.6. How would you monitor this patient intraoperatively?

Monitoring should include blood pressure, electrocardiogram, rectal temperature, precordial stethoscope, pulse oximeter, and an end-tidal CO_2 monitor.

C.7. How does the pulse oximeter function?

The commonly used pulse oximeter (Nellcor pulse oximeter Model 100) combines the scientific principles of spectrophotometric oximetry and plethysmography. Light of two wavelengths, 660 nm (red) and 925 nm (infrared), is emitted by a pair of light-emitting diodes and is passed through the tissue being measured to a photodetector. Because the saturated hemoglobin absorbs more blue light than unsaturated hemoglobin, the absorption of light for each color is an indication of the ratio of oxygen saturated blood to unsaturated blood. The pulsating vascular bed, by expanding and relaxing, creates a change in light-path length that modifies the amount of light detected. The microprocessor-controlled circuitry in the unit senses the pulsatile waveform, which is solely produced by the arterial blood, thereby allowing measurement of pulse rate and arterial saturation. The oximeter is reliably accurate in 50% to 100% saturation range.

Barash PG, Cullen BF, Stoelting RK, et al. eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:700–702.

Instruction manual. *Nellcor pulse oximeter model N-100, instruction manual*. Hayward, CA: Nellcor Inc; 1984.

Tremper KK, Barker SJ. Pulse oximetry. *Anesthesiology*. 1989;70:98–108.

C.8. What factors affect the measurement of oxygen saturation by the pulse oximeter?

Dysfunctional hemoglobin, as with carboxyhemoglobin and methoxyhemoglobin, can affect the accuracy of the oximeter. Intravascular dyes such as cardiogreen can also interfere with the accuracy of the instrument. Skin color, tissue thickness, venous blood, light intensity, and ambient light do not affect the accuracy of the instrument because they do not pulse.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:700–702.

Instruction manual. *Nellcor pulse oximeter model N-100, instruction manual*. Hayward, CA: Nellcor Inc; 1984.

Tremper KK, Barker SJ. Pulse oximetry. *Anesthesiology*. 1989;70:98–108.

D. Postoperative Management

D.1. What are the complications that can occur in the postanesthesia recovery period?

The patient should be carefully observed for signs of respiratory depression and periods of apnea secondary to combination of metabolic alkalosis, general anesthesia, and decreased body temperature. However, these infants do not appear to be at increased risk for postoperative apnea. Hypoventilation predisposes to atelectasis. Patient should be awake and responsive to avoid aspiration. Severe hypoglycemia resulting from depletion of liver glycogen stores has been reported 2 to 3 hours after surgery. Postextubation "croup" is a potentially dangerous complication in this age group.

Davis PJ, Cladis FP, Motoyama EK, eds. Associated problems in pediatric anesthesia. In: *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia: Mosby; 2011:1282–1288.

Hammer G, Hall S, Davis PJ. Anesthesia for general abdominal, thoracic, urologic, and bariatric surgery. In: *Smith's Anesthesia for Infants and Children*. 7th ed. Philadelphia: Mosby; 2006:685–722.

D.2. How would you treat postextubation "croup" in this infant?

Treatment of the potentially catastrophic postextubation laryngeal edema should be immediate, vigorous, and carried out under direct observation of the anesthesiologists. It consists of the following:

- Increasing inspired oxygen concentration (50% to 60%)
- Humidification of inspired gases
- Adequate hydration using parenteral fluids
- Light sedation to calm the patient and allow for cooperation in therapy
- Avoidance of any significant respiratory depression
- Epinephrine through hand-held nebulizer and mask, 50 μg/kg/minute of active isomer
  - Racemic epinephrine (2.25%) 0.05 mL per kg diluted in 5-mL saline solution delivered in 10 minutes

Treatment should be given over 10 minutes and may be repeated every 30 minutes, as necessary. Rebound phenomenon may be expected approximately 2 hours after cessation of this therapy.

- Steroids—dexamethasone, 0.5 to 1 mg per kg intravenously
- Reintubation—if signs of deterioration or hypoxia appear
- Tracheostomy, if necessary—rarely, subglottic edema may be so rapid and so severe that tracheostomy is the only choice

The age group most likely to manifest this complication is 1 to 4 years. Infants younger than 1 year are at most risk, mainly because of the size of the airway. Fortunately, an infant of this age is most amenable to early and vigorous intervention and should always be treated as an emergency requiring the continued presence of and evaluation by a physician who is adept at securing an airway for the child.

Davis PJ, Cladis FP, Motoyama EK, eds. Associated problems in pediatric anesthesia. In: *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia: Mosby; 2011:365–394.

Hall S. The child with a difficult airway: recognition and management. *ASA annual meeting refresher course lectures*. Park Ridge, IL: American Society of Anesthesiologists; 2006:412.

CHAPTER 41

Inflammatory Airway Disease in Childhood: Laryngotracheobronchitis

MILES DINNER

A 3-YEAR-OLD BOY was brought to the emergency room because of respiratory distress. He was noted to have stridor with substernal retractions and excessive drooling. He complained of a sore throat and had a fever of 39.5° C (103.1° F).

A. Medical Disease and Different Diagnosis

1. What portion of the airway is affected in the croup syndrome and why?
2. What is stridor?
3. How does stridor correlate with anatomic location?
4. Define croup. What is the clinical presentation of laryngotracheitis?
5. What is the differential diagnosis of acute upper airway obstruction in children?
6. What is bacterial tracheitis?
7. What congenital problems can mimic features of croup?
8. How is the severity of croup assessed?
9. What is the medical management of croup? Does this have implications for the anesthesiologist?
10. What is epiglottitis? What are its common causes? What is the incidence?
11. What are the clinical manifestations of epiglottitis?
12. How is the diagnosis of epiglottitis made?
13. What is postextubation croup? How is it managed?
14. What are the nonacute causes of partial airway obstruction in children?

B. Preoperative Evaluation and Preparation

1. Is intubation always required in children with epiglottitis?
2. Why is general anesthesia administered to a child with epiglottitis?
3. How would you prepare the patient for anesthesia?

C. Intraoperative Management

1. How is the airway of the child with epiglottitis best secured?
2. How would you induce anesthesia?
3. Should a child with epiglottitis undergo a rapid-sequence induction?
4. Is awake intubation a practical alternative to secure the patient's airway?
5. What would you do if the airway cannot be secured with intubation?
6. Should this patient have a nasotracheal or orotracheal tube placed?
7. Shortly after intubation, frothy secretions were obtained on suctioning the endotracheal tube. What is the reason for this? How can this be treated?

D. Postoperative Management

1. How long should this patient remain intubated? What criteria determine extubation time?
2. How would you make this patient comfortable during the course of intubation?
3. What outcome can one expect for the child with acute epiglottitis?

A. Medical Disease and Differential Diagnosis

A.1. What portion of the airway is affected in the croup syndrome and why?

The subglottis is typically involved in infants and children presenting with classic croup. The *subglottis* is defined as the segment of the upper airway directly below the vocal cords fusing with the upper trachea. It contains pseudostratified columnar respiratory epithelium, which is loosely adherent and prone to swelling. Because this area is fully cartilagenized in childhood, it lacks the ability to expand and thus can produce early symptoms due to even small degrees of inflammation.

Sobol SE, Zapata S. Epiglottitis and croup. *Otolaryngol Clin North Am*. 2008;41:551.

A.2. What is stridor?

Stridor is the high-pitched adventitious sound produced in the respiratory cycle by the turbulent flow of respiratory gases through a segmental narrowing in the airway. It can be biphasic, inspiratory, or expiratory, depending on the anatomic location.

A.3. How does stridor correlate with anatomic location?

Inspiratory stridor is characteristic of laryngeal or supraglottic obstruction. Such conditions as laryngeal papillomatosis, laryngeal web, laryngomalacia, and vocal cord paresis produce inspiratory stridor. Expiratory stridor is usually typical of intrathoracic processes such as extrinsic tracheal compression by a vascular ring or mass, tracheomalacia, or bronchotracheitis. Biphasic stridor is indicative of lesions or infections involving both the larynx and subglottis such as the croup syndrome, subglottic stenosis, or intralaryngeal masses.

A.4. Define croup. What is the clinical presentation of laryngotracheitis?

Croup is a generalized term referring to infections of the upper respiratory tract with a characteristic cough, inspiratory stridor, and possible respiratory distress. Other terms, namely *laryngotracheobronchitis*, *spasmodic croup*, and *bacterial tracheitis*, are

interwoven within the croup syndrome but have specialized meanings. For instance, spasmodic croup suggests a noninfectious inflammatory process as opposed to the viral etiology of laryngotracheobronchitis. Most cases occur during the colder months. There is a 2:1 male to female prevalence. Also known as *laryngotracheobronchitis* because of the structures involved, croup is usually caused by the *Haemophilus parainfluenzae* virus type 1, although type 2 and 3 may cause disease. Recently, human corona virus has been implicated in croup. It affects children between 1 and 3 years of age, with a median age of 18 months. It manifests subacutely as an exacerbation of cold symptoms with low fever, barking cough, and hoarseness. Exudative inflammation of the upper airway may cause dyspnea and in extreme cases can lead to exhaustion and frank hypoxia. In most cases, it is self-limited and benign.

Rosychuk RJ, Klassen TP, Metes D, et al. Croup presentations to emergency departments in Alberta, Canada: a large population study. *Pediatric Pulmonology.* 2010;45:83–91.

Vander Hook L, Sue K, Ihorst G, et al. Human coronaviaus NL6S infection is associated with croup. *Adv Exp Med Biol.* 2006;581:485–491.

A.5. What is the differential diagnosis of acute upper airway obstruction in children?

A full differential for this condition involves a host of infectious causes. Among the most important are bacterial tracheitis, diphtheria, retropharyngeal abscess, peritonsillar abscess, measles, and Epstein-Barr viral infection. Other causes to be considered are thermal burns, foreign body aspiration, laryngeal fractures, angioneurotic edema, vocal cord paralysis, and uvulitis.

Wald EL. Croup, common syndromes and therapy. *Pediatr Ann.* 2010;39:15–21.

A.6. What is bacterial tracheitis?

This is a severe and potentially fatal disease of an infectious nature occurring as a consequence of infection with *Staphylococcus aureus*, various streptococcal species, and *Haemophilus (H) influenzae*. It occurs in colder weather in young children as a secondary complication of viral laryngotracheitis. Although presenting the same symptoms as epiglottitis, it tends not to evolve as rapidly, and generally does not have odynophagia and drooling, two characteristic signs of epiglottitis. Most of these children require intubation for thick and difficult-to clear-secretions and during endoscopy, subglottic edema with mucosal ulceration is seen.

Wald, EL. Croup: Common syndromes and therapy. *Pediatr Ann.* 2010;39:15–21.

A.7. What congenital problems can mimic features of croup?

A host of anatomic problems can share similar signs and symptoms with the infectious agents causing airway compromise. It is only by the absence of fever and the chronicity of the situation that these are distinguishable. Vocal cord paralysis, laryngeal webs, laryngomalacia, subglottic masses (hemangiomas), and stenosis, as well as vascular anomalies are to be included.

Wald, EL. Croup: Common syndromes and therapy. *Pediatr Ann.* 2010;39:15–21.

A.8. How is the severity of croup assessed?

One evaluates the following parameters in assessing severity of the illness: (1) Work of breathing: Is there tachypnea and or retractions? (2) Chest wall motion: Is the tidal volume adequate with inspiration? (3) Overall appearance: Is the child cyanotic, obtunded, or comfortable? (4) Vocal quality: Is there stridor, diminished voice, or cry? Severe croup unresponsive to the medical therapy may require tracheal intubation. Once the diagnosis of croup has been established, the child is given a croup score, which helps determine therapy (Table 41.1).

Westley CR, Cotton EK, Brooks JG. Nebulized racemic epinephrine by IPPB for the treatment of croup: a double-blind study. *Am J Dis Child.* 1978;132:484.

A.9. What is the medical management of croup? Does this have implications for the anesthesiologist?

Mild croup is treated with inspired gas humidification, hydration, and oxygen to improve the attendant hypoxemia. Croup tents, croupettes, and blow-by oxygen are helpful. Steroids and racemic epinephrine are the prime modalities of therapy. If the patient has moderate retractions and appears dyspneic, 0.5 mL of a 2.25% racemic epinephrine solution in 2.5 mL of normal saline can be administered via nebulizer.

Airway resistance can be high with the reactive transudation and intraluminal narrowing. By vasoconstricting the arterioles of the mucosal vasculature, racemic epinephrine relieves edema. The epinephrine is prepared as a mixture of the L and D isomers to limit cardiac stimulation. Patients improve markedly, but the clinician should be cautioned that the relief may be short lived and rebound airway compromise may occur after the epinephrine wears off. The *Beta* 2 activity will cause bronchial smooth muscle relaxation. Avoid racemic epinephrine in children with glaucoma and ventricular outflow obstruction.

Dexamethasone and budesonide when given early in viral croup can be beneficial in reducing inflammation and alleviating symptoms. This takes time to work, however, requiring hours for effective onset. The pediatric dose of dexamethasone is 0.6 mg per kg orally or intramuscularly. Clinical evaluation of topical steroids

Table 41.1 The Westley Croup Score

	0	1	2	3	4	5
Cyanosis	none	—	—	—	With agitation	At rest
Level of Consciousness	Normal, including sleep	—	—	—	—	Disoriented
Stridor	None	With agitation	At rest	—	—	—
Air entry	Normal	Decreased	Markedly decreased	—	—	—
Retractions	None	Mild	Moderate	Severe	—	—

Mild croup has a score <2, moderate is between 3 and 7, and severe has a score >8.

such as budesonide has shown effective improvement, especially with laryngeal edema. Nebulized budesonide has been shown to be as effective as dexamethasone in treatment.

Behrman RE, Kliegman RM, Jensen HB, et al., eds. *Nelson Textbook of Pediatrics*. 18th ed. Philadelphia: WB Saunders; 2007:1763.

Eboriadov M, Chryssanthopoulou D, Stamodis P, et al. The effectiveness of local corticosteroid therapy in the management of mild to moderate croup. *Minerva Pediatr*. 2010:62:23–28.

A.10. What is epiglottitis? What are its common causes? What is the incidence?

Epiglottitis is an inflammation of the epiglottis usually secondary to an infectious process. It can involve other supraglottic structures such as the arytenoid, false cords, and posterior tongue leading to obstruction of the airway. Progression of swelling can rapidly lead to complete airway occlusion and death. Table 41.2 contrasts epiglottitis with croup. Epiglottitis is most often bacterial in origin. The causative agent used to be *H. influenzae* type B. However the vaccine has resulted in a remarkable decline. *Streptococcus pneumoniae* also has been infrequently associated with epiglottitis, and recently, group A beta-hemolytic streptococci have been on the increase. Burn injury, neoplastic infiltration, caustic ingestion, lymphoproliferative disease, and angioneurotic edema are other causes. The incidence has declined to 1.8 per 10,000 admissions at the Children's Hospital of Philadelphia after the *H. influenzae* B vaccine. In one study, five cases of epiglottitis occurred among children who had been immunized.

A recent retrospective review reaffirms that epiglottitis remains a significant problem in the United States, with nearly 4,000 admissions in 2006. The demographics of the disease have shifted away from that of predominantly pediatric nature to one of adulthood. The mean age in the study period from 1998 to 2006 surprisingly was 45 years old and the mortality was 36%.

D'Agostino J. Pediatric airway nightmares. *Emerg Med Clin North Am*. 2010;28:199–226.

Shah RK, Roberson DW, Jones DT. Epiglottitis in the Haemophilus influenzae type B vaccine era: changing trends. *Laryngoscope*. 2004;114:557.

Shah RK, Stocks C. Epiglottitis in the United States: national trends, variances, prognosis, and management. *Laryngoscope*. 2010;120:1256–1262.

Table 41.2 Characteristics of Croup and Epiglottitis

	CROUP	EPIGLOTTITIS
Etiology	Parainfluenza virus	*Haemophilus influenzae*
Age	4 months to 2 years	2 to 5 years
Onset	Subacute exacerbation of preexistent URI	Acute
Temperature	Low-grade fever	High fever
Course	Usually mild, stridor may worsen at night	Rapid progress of symptoms
Symptoms	Barky cough, stridor	Dysphagia, sore throat Dysphonia, respiratory distress

URI, upper respiratory infection

A.11. What are the clinical manifestations of epiglottitis?

This illness presents acutely in the otherwise healthy child between 2 and 5 years of age with fever as high as 40° C. Within a few hours, the epiglottic inflammation progresses and the child becomes dyspneic. The child sits forward to use the accessory muscles of respiration and complains of a fullness and pain in the throat. Speech sounds are muffled, known as a "hot potato voice." Salivation often is characteristic and swallowing is difficult. The child appears anxious and concentrates only on breathing. The barking cough of croup usually is absent. The older child will assume a tripod posture with the neck extended to maximize air entry. As the child fatigues, cyanosis leading to complete asphyxia may ensue without intervention. Inspiratory effort is maximal with severe airway compromise, and negative pressure pulmonary edema can occur. Chest auscultation may reveal decreased breath sounds.

Kliegman RE, Behrman RE, Jensen HB, et al., eds. *Nelson Textbook of Pediatrics*. 18th ed. Philadelphia: WB Saunders; 2007:1763.

A.12. How is the diagnosis of epiglottitis made?

Acute epiglottitis is a dire emergency and any child whose clinical presentation warrants the diagnosis of epiglottitis must be evaluated promptly in a hospital. Pharyngoscopy to visualize an inflamed epiglottis should not be attempted in an office setting, because this can stimulate upper airway reflexes and lead to increasing dyspnea. All medical centers should have in place a management protocol that standardizes the approach to this rapidly progressive and fatal disease and that involves a team of physicians and nurses from the specialties of pediatrics, otolaryngology, and anesthesiology. A logical approach is as follows:

- The child is kept calm with a parent in attendance at all times. Supplementary oxygen, maintenance of a sitting position, and reassurance are essential.
- If the patient clinically conforms to a classical presentation of epiglottitis, the operating room is alerted and the child is taken there immediately for intubation.
- With other diagnostic considerations, such as a foreign body in the upper airway, retropharyngeal abscess, congenital anomalies, and croup, the child may be escorted to radiology. The time taken for the x-ray examination obviously should be avoided in the critically ill child. A physician skilled in airway management should accompany the child with all necessary resuscitation equipment available.
- The classic thumb sign on a lateral x-ray film is an aptly named shape seen with epiglottic enlargement. However, the absence of this sign does not eliminate the diagnosis of epiglottitis. Croup is distinguished by the steeple sign representing a uniform narrowing of the subglottic airway by inflammation. Recently, magnetic resonance imaging has demonstrated the standard measurements for the hypopharyngeal space in various age groups, and it has correlated this measurement with the change produced by epiglottic inflammation. This may be a useful tool in the future to assess the severity of airway involvement.
- Laboratory evidence is nonspecific, although a high white count with bands and polymorphonuclear leukocytes is more suggestive of epiglottitis than of croup.
- Fiber-optic pharyngoscopy can be most effective if performed gently by a skilled examiner; it immediately confirms or eliminates the diagnosis. Do not perform a laryngoscopy if anxiety is increased by the procedure and hence exacerbates airway obstruction.

Kliegman RE, Behrman RE, Jensen HB, et al., eds. *Nelson Textbook of Pediatrics*. 18th ed. Philadelphia: WB Saunders; 2007:1763.

Shorten GD, Opie NJ, Graziotti P, et al. Assessment of upper airway anatomy in awake, sedated and anaesthetized patients using magnetic resonance imaging. *Anaesth Intensive Care*. 1994;22:165.

A.13. What is postextubation croup? How is it managed?

Anesthesiologists are often in the position of treating patients with postextubation airway edema, which resembles croup in its symptomatology.

Pediatric patients undergoing general endotracheal anesthesia may mimic many of the physical signs of the croup syndrome following extubation. The tracheal and subglottic mucosa have become irritated by the plastic tube, which initiates an inflammatory response, causing airway luminal narrowing. Because airway resistance is inversely proportional to the fourth power of the tracheal radius (with turbulent flow, this increases to the fifth power), the pediatric airway is especially compromised by edema. Halving the lumen will increase laminar airflow resistance 16 times.

Postextubation croup may manifest more frequently in a patient who has received large quantities of fluid or transfusions; maintained unusual or strained lateral head positioning; has a history of smoke inhalation, restrictive congenital anomalies such as a tracheoesophageal fistula, or acquired subglottic stenosis secondary to prolonged intubation as a neonate; has a coexistent upper respiratory infection, especially bronchitis; or has a cuffed endotracheal tube with high cuff pressure. The air leak test, which gauges the pressure needed to generate an audible leak in the presence of an endotracheal tube, may be predictive of postextubation stridor in children over 7 years of age.

Management involves reducing airway constriction by administering nebulized racemic epinephrine, steroids, and humidification of inspired gases. On occasion, reintubating with a soft endotracheal tube one-half to one size smaller than previously used is necessary until the inflammation subsides. Note that topical lidocaine ointment can have vasodilatory actions and should not be used in patients with postextubation croup.

Davis HW, Gartner JC, Galvis AG, et al. Acute upper airway obstruction: croup and epiglottitis. *Pediatr Clin North Am*. 1981;28:859.

Lukhassen IM, Hassing MB, Markhorst DG. Dexamethasone reduces reintubation rate due to post extubation stridor in a high-risk pediatric population. *Acta Paediatr*. 2006;95:74–76.

Mhanna MJ, Zamel YB, Tichy CM, et al. The air leak test around the endotracheal tube as a predictor of post extubation stridor is age dependent in children. *Crit Care Med*. 2002;30:2639–2643.

A.14. What are the nonacute causes of partial airway obstruction in children?

Several congenital anomalies are associated with respiratory difficulties. These can be subdivided into intrinsic and extrinsic pathologies as follows.

Extrinsic pathologies

- Cystic hygroma—a proliferation or expansion of lymphatic channels, usually in the cervical region, which can compress the airway and lead to enlargement of the tongue.
- Vascular anomalies—abnormalities of the aortic arch usually caused by aberrant vessels lead to compression of the airway. This is often position dependent and may be responsible for coughing and wheezing when the patient is supine.
- Neoplastic compression of the trachea by lymphoma, hemangioma, neurofibromatosis, rhabdomyosarcoma, and other neural tumors in the mediastinum may occur and enlarge or compress airway structures.

Intrinsic pathologies

- Subglottic stenosis—especially as acquired in previously intubated neonates. This form of airway narrowing occurs below the vocal cords, and it can lead to marked airway obstruction with respiratory infections. The congenital form may not be appreciated until an upper respiratory infection is present, when stridor may occur.
- Vocal cord paralysis—considered the second most common laryngeal anomaly in children, it is associated with the Arnold-Chiari malformation.
- Laryngeal structural anomalies—webs, laryngoceles, and cysts.

Perry H. Stridor. In: Fleisher GR, Ludwig S, Henretig FM, eds. *Textbook of Pediatric Emergency Medicine*. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2006.

B. Preoperative Evaluation and Preparation

B.1. Is intubation always required in children with epiglottitis?

Adult patients often can be managed under very vigilant intubation provided that there is no impending obstructive danger. However, contemporary practice warrants the establishing of an airway with an endotracheal tube in the vast majority of infants and children. Nasotracheal intubation most often is used for ease of maintaining the child's comfort and safety. Endoscopic evaluation using appropriate fiber-optic airway endoscopy is a major advance in the management of epiglottitis.

Acevedo JL, Lander L, Choi S, et al. Airway management in pediatric epiglottis, a national perspective. *Otolaryngol Head Neuro Surg*. 2009;140:548–551.

Damm M, Eckel HE, Jungehulsing M, et al. Airway endoscopy in the interdisciplinary management of acute epiglottitis. *Int J Pediatr Otorhinolaryngol*. 1996;38:41.

B.2. Why is general anesthesia administered to a child with epiglottitis?

General anesthesia facilitates several activities. It gives the examiner a thorough look at the supraglottic area, which would be impossible and dangerous in the awake child. In addition, endotracheal intubation can be accomplished under controlled, relaxed conditions without trauma and laryngospasm. Intubation can be difficult because of the swelling and deformation of the paraepiglottic tissues. Clinicians who have no experience with this unusual appearance will find it easier to visualize landmarks and secure the airway when the patient is in a surgical plane of anesthesia.

Diaz JH. Croup and epiglottitis in children. *Anesthesiology*. 1985;64:628.

Jenkins IA, Saunders M. Infections of the airway. *Pediatric Anesth*. 2009;19:118–130.

B.3. How would you prepare the patient for anesthesia?

Expedience is crucial. Once the diagnosis is made and the operating room alerted, the child is transported accompanied by his or her parents and a physician with airway supportive equipment. It is not necessary to place an intravenous line, because this can be done more easily under anesthesia without upsetting the child. Any maneuver that causes the child to cry will potentially interfere with breathing. The child should, therefore, be kept calm and constantly reassured. Nasal prong or face tent oxygen should be provided and portable pulse oximetry should be used.

Equipment, which is prepared in the operating room, includes a suitable mask and endotracheal tube, sized two gauges (1-mm diameter) smaller than normally expected. Lidocaine, succinylcholine, atropine, and ketamine in convenient dilutions should be readily available. A cricothyrotomy tray should be available as a precaution.

The parent is dressed in operating room attire to accompany the child into the operating room. Before induction, the parent is instructed on his or her role in comforting the child, encouraging complicity with mask breathing, and gently holding the child when the inhalation induction commences. The parent also should be told that as the child begins to fall asleep, he or she will be asked to leave the room. For anesthesiologists unaccustomed to the presence of parents in the operating room, the extra anxiety created by parental presence can be attenuated by having them depart just as the patient begins to get sleepy. When parents can provide their assistance in an emotionally controlled, supportive way, a smooth, safe anesthetic induction usually can be well facilitated. A Hudson mask can also be used if hooked up to the outflow portion of the anesthesia machine to facilitate mask induction.

Berry FA. Management of the pediatric patient with croup or epiglottitis. *ASA Annual Meeting Refresher Course Lectures*. Park Ridge, IL: American Society of Anesthesiologists; 1990:261.

Tan GM. New way to mask induce a child. *Paediatric Anesth*. 2002;12:742.

C. Intraoperative Management

C.1. How is the airway of the child with epiglottitis best secured?

Little debate occurs over the safety and efficacy of endotracheal intubation provided that supportive staff is readily available. The endotracheal tube should be sized down 0.5 mm or 1.0 mm due to the inherent swelling and to protect against postextubation complications. Thick, copious secretions must be cleared frequently to prevent obstruction, and the child must be sedated to tolerate the endotracheal tube and to keep it secure in place. In the smaller hospital without a pediatric intensive care facility or experienced personnel, a tracheotomy may be the safest route.

C.2. How would you induce anesthesia?

Verbal assurance is constantly given. The child is seated on the parent's lap in the operating room and is preoxygenated. Sevoflurane is a good choice of induction agent because it is less pungent than other irritative gases like desflurane and is usually well tolerated without a high incidence of laryngospasm, coughing, or other irritative reflexes. The inhalational agent should be initiated slowly and increased in concentration as tolerated. A flavored mask with a pleasant scent may be helpful to enlist the child's cooperation. As the child tires, the supine position is assumed. If there are any considerations of gastric content regurgitation either due to a recent meal or antecedent history of reflux, cricoid pressure is applied as a safeguard against aspiration. The patient may undergo a brief period of excitement during which care is taken not to be overly zealous with ventilatory assistance. Spontaneous, unassisted ventilation should continue as an intravenous line is started. Glycopyrrolate 0.01 mg per kg is given intravenously as an antisialagogue. Ventilatory assistance but not control can be initiated to limit hypercarbia. End-tidal gas analysis is monitored continually and the airway is adjusted to provide maximal tidal exchange. Sevoflurane concentration is increased as tolerated to 8%, provided cardiovascular stability is maintained to achieve adequate depth of anesthesia. Airway obstruction will decrease ventilation and anesthetic uptake, requiring longer induction time.

When the patient is in a deep plane of anesthesia (remember that the minimal alveolar concentration of sevoflurane in children is higher than in adults), a careful laryngoscopy is carried out. Paralysis is unnecessary in this deep plane of anesthesia. However, if several attempts are required with the possibility of the patient becoming light and reactive, a small dose of a neuromuscular blocker (e.g., rocuronium 0.4 mg per kg) will serve to maintain stable intubating conditions. This should be given only after it has been shown that the patient can be ventilated with a bag and mask.

DeSoto H. Anesthesia for pediatric ENT surgery—routine and emergent. *ASA Annual Meeting Refresher Course Lectures*. Park Ridge, IL: American Society of Anesthesiologists; 2000:252.

Hall SC. The child with a difficult airway: recognition and management. *ASA Annual Meeting Refresher Course Lectures*. Park Ridge, IL: American Society of Anesthesiologists; 2006:412.

Spalding MB, Ala-Kokko TI. The use of inhaled sevoflurane for endotracheal intubation in epiglottitis. *Anesthesiology*. 1998;89:1025.

C.3. Should a child with epiglottitis undergo a rapid-sequence induction?

In the child with a full stomach, a mask induction leaves the airway unprotected from aspiration of gastric contents. However, a rapid-sequence induction may predispose the patient to severe hypoxia and hypoventilation should the clinician not be able to intubate expediently. Because the supraglottic landmarks are distorted by erythema and edema, recognition of the glottic inlet is obscured. In the spontaneously breathing patient, small air movements and the resultant secretional bubbling may highlight the glottic opening. In addition, paralysis in no way secures ventilatability.

If the patient must be manually ventilated, it is possible to meet with complete obstruction secondary to invagination of the swollen supraglottic tissues into the laryngeal introitus. In such a case, positive end-expiratory pressure or the jaw-thrust maneuver may fail to correct the airway obstruction.

Should the child be too agitated to cooperate with an inhalational induction, an intramuscular dose of ketamine (2 to 3 mg per kg) will accomplish sedation and preserve ventilation. However, it may accentuate airway reflexes, and the clinician should be wary of laryngospasm. Videolaryngoscopy with the various available modalities has improved laryngeal visualization, but these remain limited in their use.

DeSoto H. Anesthesia for pediatric ENT surgery—routine and emergent. *ASA Annual Meeting Refresher Course Lectures*. Park Ridge, IL: American Society of Anesthesiologists; 2000:252.

Hall SC. The child with a difficult airway: recognition and management. *ASA Annual Meeting Refresher Course Lectures*. Park Ridge, IL: American Society of Anesthesiologists; 2006:412.

Nagler J, Bachur RG. Advanced airway management. *Curr Opin Pediatr*. 2009:299–305.

C.4. Is awake intubation a practical alternative to secure the patient's airway?

Some authors suggest awake intubation with topical anesthesia. In such cases, the anesthesiologist should be alerted to the possibility of adenoidal bleeding, difficult visualization, agitation, trauma, and compromised ventilation. Unless one has acquired great skill at awake pediatric intubation in the child with a normal airway, this technique should be avoided in these patients. In the adult, the awake glidescope intubation has been reported with success.

Diaz JH. Croup and epiglottitis in children. *Anesthesiology.* 1985;64:628.

Sinofsky AH, Milo SP, Scher C. The awake glidescopic intubation: an additional alternative to the difficult intubation. *Middle East Anesth.* 2010;20:743–746.

C.5. What would you do if the airway cannot be secured with intubation?

Preemptive caution is critical and an ENT (ear, nose, and throat) surgeon should be available. In the event that the airway is lost, percutaneous transtracheal ventilation can be performed. This involves inserting a needle through the cricothyroid membrane as follows. Localize the cricothyroid membrane and topically cleanse the area with antiseptic. Anesthetize the skin with lidocaine (if time permitting) and then insert a 16-gauge catheter (attached to needle) in the midline in the inferior portion of the cricothyroid membrane and directed caudally. Attach a 3-mL syringe to the needle barrel applying negative pressure. If the syringe contains a few milliliters of saline, air bubbles will be apparent when the trachea is entered. Following entry, advance the catheter into the trachea. Depending on the hub size, a 3.0-mm or 3.5-mm endotracheal tube adapter can be inserted into the catheter to interface with an Ambu bag. Alternatively, a 6.5-mm or 7.0-mm endotracheal tube adapter can be inserted into a 3-mL syringe without the plunger to interface with an Ambu bag or anesthesia circuit (Fig. 41.1). Jet ventilation can also be applied with high-pressure tubing keeping careful observation of respiratory dynamics and saturation. A tracheotomy in skilled hands also can be performed.

Delaney WA, Kaiser RE. Percutaneous transtracheal jet ventilation made easy. *Anesthesiology.* 1991;74:952.

Deutsch ES. Tracheotomy: pediatric considerations. *Respir Care.* 2010;55:1082–1090.

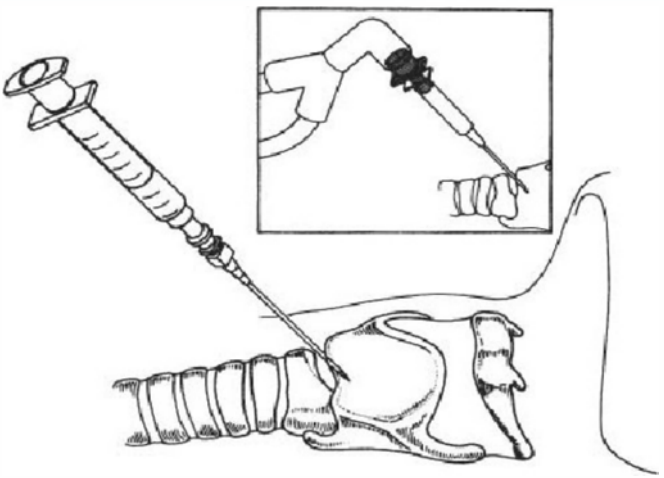

Figure 41.1 An emergency cricothyrotomy may be performed by passing a 14-gauge intravenous catheter through the cricothyroid membrane into the trachea. A 3-mL syringe with the plunger removed will accept a 15-mm endotracheal tube adapter that allows attachment of an oxygen-delivery system. (From Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia.* 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2001:1035–1041, with permission.)

C.6. Should this patient have a nasotracheal or orotracheal tube placed?

The patient will better tolerate a nasal endotracheal tube for prolonged intubation. Oropharyngeal toilet also will be easier. However, because the intubation can be difficult with epiglottitis and may predispose the patient to the problems listed in section C.4, the orotracheal route is easier and safer. Once the airway is secured orally, a nasotracheal tube can be inserted with laryngoscopic guidance.

C.7. Shortly after intubation, frothy secretions were obtained on suctioning the endotracheal tube. What is the reason for this? How can this be treated?

Davis et al. describes 7% of these patients as having pulmonary edema after intubation. This phenomenon relates to the transudation into the alveoli during periods of increased transpulmonary pressure. This occurs especially during obstructed inspiration. If the obstruction is complete, it is referred to as the "Müller" maneuver. The high negative pressures are buffered by the decreased venous return during exhalation. However, relief of the airway obstruction facilitates the extravasation of fluid for an increased venous return.

Treatment of this negative pressure pulmonary edema requires positive end-expiratory pressure. Diuretics and fluid restriction are not required because this condition generally is self-correcting. This can be administered by nasal bilevel means, mask continuous pressure, or intubation.

da Silva, Lucas MD, Neto HM, et al. Negative-pressure pulmonary edema: A rare complication of upper airway obstruction in children. *Ped Emerg Care.* 2005;21:751–754.

Davis HW, Gartener JC, Galvis AG, et al. Acute upper airway obstruction: croup and epiglottitis. *Pediatr Clin North Am.* 1981;28:859.

D. Postoperative Management

D.1. How long should this patient remain intubated? What criteria determine extubation time?

Earlier studies have shown a mean intubation duration of 36 hours in 23 patients with a range of 19 to 67 hours. These patients were treated with ampicillin or chloramphenicol and the epiglottis was visualized before extubation. The current antibiotic regimen is cefazolin 75 to 100 mg/kg/day in three divided doses or clindamycin 30 to 40 mg/kg/day in three divided doses with the addition of a third-generation cephalosporin such as cefotaxime or ceftriaxone.

Criteria for extubation include an increased air leak around the endotracheal tube as well as decreased erythema and edema. Vernon and Sarnaik, however, feel that instrumentation and examination of the child is unnecessary and extubation at 36 to 48 hours can be accomplished easily in all patients. Hopkins recommended that the flexible fiber-optic laryngoscope be used to visualize the epiglottis and determine extubation time.

Damm M, Eckel HE, Jungehulsing M, et al. Airway endoscopy in the interdisciplinary management of acute epiglottitis. *Int J Pediatr Otorhinolaryngol.* 1996;38:41.

Hopkins RL. Extubation in epiglottitis. *Anesth Analg.* 1984;63:468.

Rothstein P, Lister G. Epiglottitis: duration of intubation and fever. *Anesth Analg.* 1983; 62:785.

Vernon DD, Sarnaik AP. Extubation in epiglottitis. *Anesth Analg.* 1984;63:469.

D.2. How would you make this patient comfortable during the course of intubation?

The child must be kept sedated to minimize movement, to prevent deliberate extubation, and to provide anxiolysis. Midazolam (0.075 mg per kg) as a starting dose titrated upward to effect followed by a continuous infusion of 0.04 mg/kg/hour will be effective in this regard. If necessary, a fentanyl infusion (1 to 2 μg/kg/hour) can be supplemented. Alternatively, a short course of propofol can be given as a drip. A bilateral superior laryngeal nerve block in experienced hands allows for better endotracheal tube toleration.

Of course, respiratory care, humidification, suctioning, and secretion mobilization must receive attention.

D.3. What outcome can one expect for the child with acute epiglottitis?

Residual airway problems are unusual in the vast majority of children. Most children who are diagnosed in time and intubated go on to a full recovery without sequelae. Complications include associated pneumonia, respiratory failure, hypoxia, and cardiac arrest.

CHAPTER 42

Cleft Palate

AARTI SHARMA

A 3-MONTH-OLD MALE INFANT

was scheduled for repair of a cleft lip and a cleft palate. According to his pediatrician, the infant was born at full term and had no other medical problems.

A. Medical Disease and Differential Diagnosis

1. Describe the anatomic concept of a cleft palate and a cleft lip.
2. What is the cause of a cleft lip or a cleft palate?
3. What is the incidence of a cleft lip and a cleft palate?
4. Discuss the pathophysiology of a cleft lip and palate in the neonate and in the older child (e.g., age >5 years).
5. What other conditions are associated with a cleft lip and a cleft palate?
6. What is Pierre Robin syndrome?
7. What is Treacher Collins syndrome?
8. What kind of specialized team care would these patients need?
9. Discuss indications and timing of closure of a cleft lip and palate.
10. What is velopharyngeal incompetence and how can it be diagnosed?
11. What is the relation of tonsillectomy and adenoidectomy to velopharyngeal incompetence?

B. Preoperative Evaluation and Preparation

1. What information do you need before closure of a cleft lip and palate?
2. What preoperative orders are needed?

C. Intraoperative Management

1. What monitors will you need for cheiloplasty and palatoplasty?
2. Discuss the induction and the anesthetic management for cleft lip and palate.
3. What positioning is recommended for cleft palate repair surgery?
4. What are the reported complications of this type of surgery and anesthesia?
5. Briefly describe the surgical techniques used to repair cleft defects.

6. How does a pharyngeal flap affect anesthetic management or any subsequent anesthetic administered to this patient?
7. What is an Abbe flap? What are its anesthetic implications?
8. What is the crucial problem of anesthesia for cleft palate? What are the unique considerations of this surgical repair?
9. What is laryngospasm? How would you make a diagnosis of laryngospasm?
10. How would you manage the patient with laryngospasm?

D. Postoperative Management

1. What complications of cleft lip and cleft palate surgery may be seen in the recovery room?
2. How do you protect the airway postoperatively?
3. How would you control postoperative pain in patients following a cleft lip and a cleft palate repair?

A. Medical Disease and Differential Diagnosis

A.1. Describe the anatomic concept of a cleft palate and a cleft lip.

Congenital clefts of upper lip occur because of failure of fusion of the maxillary and the medial and the lateral nasal processes. They vary from notch in the upper lip to a cleft through the lip and the floor of the nose involving the alveolar ridge, or they may be complete cleft of the lip and the palate.

The cleft palate is divided into prepalatal and postpalatal clefts. The incisive foramen marks the boundary between the two. They both have different embryologic development. Prepalatal cleft involves anterior palate, alveolus, lip, nostril floor, and ala nasi. Postpalatal clefts may extend anywhere from soft and hard palate to the incisive foramen. The third type is a submucosal cleft in which a bone defect exists without a mucosal defect. The most common cleft of the palate is a left complete cleft of the prepalatal and palatal structures. The second most common is a midline cleft of all the soft palate and part of the hard palate without a cleft in the prepalatal area. Various degrees of the cleft palate and lip are shown in Figure 42.1.

Aston SJ, Bartlett SP, Beasley RW, et al., eds. *Grabb and Smith's Plastic Surgery*. 6th ed. Lippincott Williams & Wilkins; 2007:179–190.

Gregory GA, ed. *Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 2002:731.

A.2. What is the cause of a cleft lip or a cleft palate?

Major components of face develop between 4 and 7 weeks of fetal life. There are three mesodermal islands, one central and two lateral. Prepalatal clefts are caused by the failure of these mesodermal elements to develop and fuse. Palatal clefts are caused when the palatal ridges fail to migrate medially, contact, and fuse (Fig. 42.1).

Aston SJ, Bartlett SP, Beasley RW, et al., eds. *Grabb and Smith's Plastic Surgery*. 6th ed. Lippincott Williams & Wilkins; 2007:179–190.

A.3. What is the incidence of a cleft lip and a cleft palate?

Cleft lip and cleft palate may occur together or separately. A cleft lip with or without a cleft palate occurs in 1:1,000 births. A cleft palate alone occurs in approximately

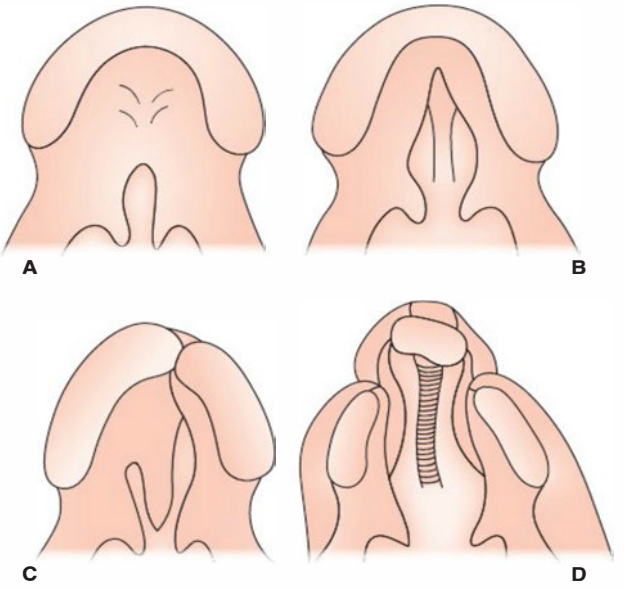

Figure 42.1 Various degrees of cleft palate and lip. **A.** Cleft of the soft palate only. **B.** Cleft of the soft and hard palate as far forward as the incisive foramen. **C.** Complete unilateral alveolar cleft, usually involving the lip. **D.** Complete bilateral alveolar cleft, usually associated with bilateral clefts of the lip. (Adapted from McCarthy JG, ed. Cleft lip and palate and craniofacial abnormalities. In: *Plastic surgery.* Vol 4. Philadelphia: WB Saunders; 1990.)

1:2,500 births. A cleft lip with or without a cleft palate is more common in boys, whereas isolated cleft palate is more common in girls.

The highest incidence of a cleft lip and a cleft palate occurs among Asians (1.61:1,000 births), whereas the lowest incidence is in African Americans (0.3:1,000 births). The incidence in whites is intermediate (0.9:1,000 births).

Samanich J. Cleft palate. *Pediatr Rev.* 2009;30:230–232.

A.4. Discuss the pathophysiology of a cleft lip and palate in the neonate and in the older child (e.g., age >5 years).

Cleft palate is responsible for some major physiologic disorders. The pharynx communicates more extensively with the nasal fossae and the oral cavity. The complex mechanisms of swallowing, breathing, hearing (through the eustachian tube), and speech are, therefore, impaired.

The presence of a cleft lip and palate in a neonate results in feeding difficulties. The neonate cannot suck because the cleft makes the creation of a negative pressure difficult. Breast-feeding is improbable and bottle-feeding is difficult.

Essentially, all children with a cleft palate have middle ear disease because abnormal anatomy of the nasopharynx adversely affects eustachian tube function. Chronic middle ear effusion produces varying degree of conductive hearing loss. Nasal septation between food and air is absent, creating a nonphysiologic mixing chamber in the nasopharynx. Not infrequently, this is associated with chronic rhinorrhea that must be distinguished preoperatively from infection.

Secondary defects of tooth development, growth of the ala nasi, and velopharyngeal function (contact between the soft palate and the posterior pharynx for speech and swallowing) can also occur.

Psychologic problems may be considerable as this youngster approaches school age and peer association. The speech of these children is typically nasal with an inability to sound the so-called plosives (*p*/*k*/*d*/*t*) and fricatives (*s*/*f*).

Malek R, ed. Cleft lip and palate, lesions, pathophysiology and primary treatment. London: Martin Dunitz; 2001:124–130.

A.5. What other conditions are associated with a cleft lip and a cleft palate?

Associated anomalies occur 30 times more frequently in the patient with isolated cleft palate than in the noncleft population.

The most common non–syndrome-related abnormalities are umbilical hernias, clubfoot, and limb and ear deformities.

The most common syndromes associated with a cleft lip and a cleft palate are:

- Velocardiofacial (Shprintzen) syndrome
- Van der Woude syndrome
- Stickler syndrome
- Pierre Robin syndrome
- Fetal alcohol syndrome
- Goldenhar syndrome (facio-auriculo-vertebral syndrome or hemifacial microsomia)
- Treacher Collins syndrome
- Nager syndrome
- Down syndrome

Calzolari E, Pierini A, Astolfi G, et al. Associated anomalies in multimalformed infants with cleftlip and palate: an epidemiologic study of nearly 6 million births in 23 EUROCRAT registeries. *Am J Med Genet*. 2007;143:528–537.

A.6. What is Pierre Robin syndrome?

This syndrome is characterized by retrognathia or micrognathia, glossoptosis, and airway obstruction. For facial cleft surgeons, Pierre Robin syndrome is defined by a triad of clinical criteria:

- Retrognathia
- Severe respiratory and/or digestive disorders in early infancy
- Cleft palate

An incomplete cleft of the palate is associated with the syndrome in approximately 50% of these patients. In patients with micrognathia (small jaw) or retrognathia, the chin is posteriorly displaced, causing the tongue to fall backward toward the posterior pharyngeal wall. This results in obstruction of the airway on inspiration. Crying or straining by these children can often keep the airway open. However, when the child relaxes or sleeps, airway obstruction occurs. Because of these respiratory problems, feeding may become very difficult. This can lead to a sequence of events: glossoptosis, airway obstruction, crying or straining with increased energy expenditure, and decreased oral intake. This vicious cycle of events if untreated can led to exhaustion, cardiac failure, and ultimately death.

Jones KL, ed. *Smith's Recognizable Patterns of Human Malformation*. 7th ed. Philadelphia: WB Saunders; 2006:262.

A.7. What is Treacher Collins syndrome?

It is highly complex disease process consisting of

- Hypoplastic cheeks, zygomatic arches, and mandible
- Microtia with possible hearing loss
- High arched or cleft palate
- Macrostomia (abnormally large mouth)
- Antimongoloid slant to the eyes
- Colobomas (notching of the outer portion of the lower eyelid)
- Increased anterior facial height
- Malocclusion (anterior open bite)
- Small oral cavity and airway with normal-sized tongue
- Pointed nasal prominence

Jones KL, ed. *Smith's Recognizable Patterns of Human Malformation*. 7th ed. Philadelphia: WB Saunders; 2006:280–281.

A.8. What kind of specialized team care would these patients need?

These patients need a pediatrician to maintain their overall health and a surgeon and an anesthesiologist to accomplish the various surgeries. They would need a speech therapist to prevent or overcome the speech deficiencies and an orthodontist for early orthodontic intervention to develop and maintain relatively normal bite and dentition. The care team also includes geneticist, pediatric dentist, prosthodontist, psychologist, medical social worker, and public health nurse.

Nelson WE, Behrman RE, et al. eds. *Nelson Textbook of Pediatrics*. 18th ed. Philadelphia: WB Saunders; 2007:1532–1533.

A.9. Discuss indications and timing of closure of a cleft lip and palate.

Functional goals of cleft palate surgery are normal speech, hearing, and maxillofacial growth. It is thought that speech and hearing are improved by early cleft palate repair (before 24 months of age) and that the delayed closure (after 4 years) is associated with less retardation of midfacial growth. An early two-stage palate repair is advocated in management of these patients. The recommended sequence involves closure of the soft palate at 3 to 6 months of age with secondary closure of the residual hard palate at 15 to 18 months of age. This sequence takes advantage of the early physiology and growth that occurs in the soft palate, which is vital in the development of speech. Furthermore, it avoids the potential pitfalls of the growth disturbance related to early periosteal undermining of palatal and vomerine tissue. This repair sequence also provides total palatal closure before speech evolves. If soft palate is repaired at the time of lip repair, an additional anesthetic is avoided.

Malek R, ed. Cleft lip and palate, lesions, pathophysiology and primary treatment. London: Martin Dunitz; 2001:197–205.

A.10. What is velopharyngeal incompetence and how can it be diagnosed?

Velopharyngeal incompetence is inability of soft palate in fulfilling its role in closing the nasopharynx, thereby affecting the phonation seriously.

To produce plosive sounds, *p*/*k*/*t*/*d*, or the sibilants, *s*/*sh*, the soft palate must touch the posterior pharyngeal wall to close the nose. Failure of closure results in the typical hypernasal speech. The most common cause of this is the cleft palate, but patients with congenitally short palates and no cleft can also have this typical speech. Treatment consists of surgical lengthening of the palate by the pushback operation with or without pharyngeal flap. The diagnosis of velopharyngeal incompetence can be suggested by the child's speech. More objective diagnosis can be obtained by direct vision of the soft palate while the child is pronouncing certain keywords (*kah, kah*), by the fogging of the hand mirror placed under the nose during speech, and from cinefluorographic x-ray films.

In patients with velopharyngeal incompetence, videofluoroscopy and nasopharyngoscopy can provide information that will help select the appropriate procedure, either pharyngoplasty or posterior pharyngeal flap.

Dudas JR, Deleyiannis FW, Ford MD, et al. Diagnosis and treatment of velopharyngeal insufficiency: clinical utility of speech evaluation and videofluoroscopy. *Ann Plast Surg*. 2006;56(5):511–517.

A.11. What is the relation of tonsillectomy and adenoidectomy to velopharyngeal incompetence?

There is often a considerable mass of tonsillar and adenoidal tissue at the age when surgery is usually performed, and, in addition to the latent danger of infection, the flap used in pharyngoplasty creates an obstruction that seriously complicates their subsequent removal. Furthermore, bulky tonsils may hinder retrodisplacement of the soft palate or block the air flow by obstructing cavum, which has already been reduced in volume by the retrodisplacement and the presence of the flap. It is, therefore, preferable to remove the tonsils and adenoids a few months before pharyngoplasty. The parents may wonder why this decision has been made, because they have been repeatedly told that the adenoids should not be removed in case of cleft palate because this might create or aggravate velar insufficiency. However, once velar inadequacy is confirmed, the parents are in a position to understand that these precautions are no longer justified and that the adenoids can represent a source of problems if not treated with radical measures. During tonsillectomy, it is important to leave the tonsillar pillars absolutely intact, because their muscle structure has a vital physiologic role.

Malek R, ed. *Cleft Lip and Palate, Lesions, Pathophysiology and Primary Treatment*. London: Martin Dunitz; 2001:146.

B. Preoperative Evaluation and Preparation

B.1. What information do you need before closure of a cleft lip and palate?

Preoperative anesthetic evaluation is invaluable and includes the history and physical examination and suitable laboratory data. It gives a picture of the patient's general health. Hemoglobin level, which is often low in very young infants, should be obtained. If Treacher Collins or Pierre Robin syndrome is suspected, an x-ray film of the mandible may be helpful. Examination of the mouth may indicate potential intubation problems. The examination also offers a good opportunity to appraise the family environment, because parental cooperation is essential for proper postoperative care.

Most surgeons repair a cleft lip when the baby is 6 to 10 weeks old and opt to repair a cleft palate at 6 to 12 months of age. The exact age of repair will depend on the size and health of the child and the surgeon's preference.

Because periosteoplasty and lip adhesions are carried out as soon as the segments are in alignment and the surgery is less extensive, the rule of 10 can be used with moderate license:

- *Weight*. Approximately 10 lbs.
- *Hemoglobin*. 10 g/dL or more
- *White blood cell count*. Less than 10,000 per μL
- *Age*. Can be less than 10 weeks

With open cleft palate, however, it is common to have crusting and low-grade infection of the nasopharynx because of food and fluid regurgitation through the cleft. It is nearly impossible to eliminate this completely. Unless an acute inflammation process is present, this does not lead to complications.

Barrett BM Jr, ed. *Patient Care in Plastic Surgery*. St. Louis: Mosby; 1996:343–344.

B.2. What preoperative orders are needed?

Preoperative fasting has been a prerequisite for elective surgery. An issue of particular importance to the pediatric patient is the wonderful changes that have taken place regarding preoperative fasting. Recent work has shown that prolonged fasting does not reduce the risk of aspiration pneumonitis during anesthesia. This has led to reduction in the fasting times. Reduced fasting increases patient comfort and there may be less potential for intraoperative hypoglycemia. Fasting guidelines for infants and children are shown in Table 42.1.

Because multiple operations may be required, the emotional trauma of each hospital experience must be minimized. The most common premedication used at Cornell Medical Center in pediatric patients is oral midazolam. Dose can range from 0.25 to 0.5 mg per kg orally. Children younger than 8 months rarely require premedication. In children with anticipated difficulty in airway management and in those with propensity toward airway obstruction, premedication should be avoided. Special orders include antibiotics, if the infant or child has associated congenital heart disease, and the typing and crossmatching of a unit of blood for palatal surgery.

Cote CJ. Preparation, premedication and induction of anesthesia in children. *ASA Annual Meeting Refresher Course Lectures*. Park Ridge, IL: American Society of Anesthesiologists; 2001:243.

Table 42.1 Minimum Fasting Period (Hours) for Pediatric Patients

	CLEAR FLUIDS	BREAST MILK	FORMULA OR COW'S MILK	SOLIDS
Children	2	—	6	6
3–12 mo	2	4	6	6
<3 mo	2	4	4	6

C. Intraoperative Management

C.1. What monitors will you need for cheiloplasty and palatoplasty?

Heart rate, respiration, blood pressure, temperature, and oxygen saturation are monitored at all times. An electrocardiogram provides visual and audible evidence of the electrical activity of the heart. A precordial stethoscope monitors both heart and respiratory sounds. It is particularly important in this patient because once the surgery has begun, the anesthesiologist no longer has easy direct access to the airway. The use of pulse oximetry and an end-tidal CO_2 monitor is indispensable. Temperature should be monitored per rectum or axilla. A warming blanket should be used in these patients to avoid hypothermia. Blood loss determination should be made by a calibrated catchment trap in the suction line and by weighing sponges. Blood loss rarely exceeds 10% of circulating blood volume; however, properly crossmatched and screened blood should be available but used only if absolutely necessary.

C.2. Discuss the induction and the anesthetic management for cleft lip and palate.

After suitable monitors are attached, the infant is induced with oxygen, nitrous oxide, and either sevoflurane or halothane. Because cardiac depressant effects of sevoflurane are less pronounced than that of halothane, sevoflurane is preferred for induction. In addition, the myocardium is more sensitive to exogenous epinephrine with use of halothane. Recommended maximal doses of lidocaine and epinephrine for palate or lip surgery are 5 mg per kg and 10 μg per kg, respectively. This epinephrine dose is for hypocarbic or normocarbic patients.

Once the patient is asleep, an intravenous line is established and appropriate intravenous fluids are started. Intubation can be facilitated with nondepolarizing muscle relaxants such as vecuronium 0.1 mg per kg. Muscle relaxants should be withheld if any possibility of difficulty in intubation exists.

Laryngoscopy in patient with a cleft lip is generally straightforward, but the cleft palate has the capability to trap and immobilize a straight blade. Should this occur, the anesthesiologist must first recognize the problem and then consider inserting a gauze pack or a dental roll in the cleft before laryngoscopy.

To achieve a cosmetic repair, symmetry is essential, so the tube should exit the mouth in the midline without facial distortion from either the tube or the securing tape. Some surgeons prefer to suture the tube to the lower gum.

An orogastric tube should be passed to empty the stomach of gas and secretions, and it should be removed before preparation of the surgical field.

A pharyngeal pack of moistened ribbon gauze is inserted for a cleft lip repairs; as for a cleft palate repair, the surgeon inserts the gag before insertion of the pharyngeal pack. Following the gag and pack insertion, ventilation should be reassessed, because tube compression may have occurred. To avert eye injury, an ocular lubricant is placed in the eyes, and the upper eyelids are splinted shut with tape.

During the surgery, it is necessary to have good communication and cooperation between the surgeon and the anesthesiologist because the surgeon's tools and hands and the anesthesiologist's endotracheal tube and apparatus all occupy the same very small space.

Gregory GA, ed. *Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 2002:731.

C.3. What positioning is recommended for cleft palate repair surgery?

Correct positioning of the child is important for the plastic surgeon, who sits at the head of the operating table. Head extension must be maximal for cleft palate surgery.

The entire body is raised with a thick foam mat or folded blanket, allowing the head to drop back hyperextended into a stockinette head support. Not only does this position provide good exposure, but it also allows blood to flow away from the larynx and toward the nasopharynx, allowing it to be removed by suction.

C.4. What are the reported complications of this type of surgery and anesthesia?

Anesthetic complications include obstruction of the endotracheal tube, inadvertent extubation during the procedure, and cardiac arrest. Postanesthetic complications include airway obstruction, bleeding with or without aspiration, and pneumonia. Complications not related to anesthetic management are wound healing, diarrhea, and otitis media. The mortality rate has been reported to be less than 0.5%.

Gregory GA, ed. *Pediatric Anesthesia.* 4th ed. New York: Churchill Livingstone; 2002:731–732.

C.5. Briefly describe the surgical techniques used to repair cleft defects.

The Furlow procedure is the most common technique for cleft palate closure. It involves opposing z-plasties of the mucosa and the musculature of the soft palate. The goal is to separate the nonfunctioning attachments to the posterior border of the hard palate and to displace the mucosa and the musculature posteriorly.

Other basic surgical techniques include von Langenbeck technique, Schweckendiek technique, two-flap technique, three-flap/V-Y technique.

Although most of the repairs do not involve repairing the muscular sling, doing so allows better palatal and eustachian tube function.

Sadove AM, van Aalst JA, Culp JA. Cleft palate repair: art and issues. *Clin Plast Surg.* 2004;31(2):231–241.

C.6. How does a pharyngeal flap affect anesthetic management or any subsequent anesthetic administered to this patient?

The presence of this flap prohibits nasoendotracheal intubation and makes many nasal techniques difficult (e.g., insertion of nasogastric tube). The degree of obstruction is related to the width of the flap. Traumatic rupture of this flap secondary to attempted nasotracheal intubation could produce bleeding, aspiration, and laryngospasm.

Traumatic rupture of soft palate can occur from placement of laryngeal mask airway.

Knowledge of prior surgery is essential to good anesthetic management. Following the pushback and pharyngeal flap operation (pharyngoplasty), significant airway obstruction has been noted in the early postoperative period. Use of pulse oximetry during sleep state has demonstrated obstruction and desaturation in the first 48 to 72 hours.

Dearlove O, Perkins RJ, Briggs G. Anaesthesia after cleft palate repair. *Anaesthesia.* 2004;59(10):1032.

Somerville NS, Fenlon S, Boorman J, et al. Disruption of cleft palate repair following the use of the laryngeal mask airway. *Anaesthesia.* 2004;59(4):401–403.

C.7. What is an Abbe flap? What are its anesthetic implications?

An Abbe flap is a full-thickness pedicle flap taken from the lower lip and swung on its own artery to a position in the upper lip to replace a tissue deficit resulting from any

cause, such as surgical excision of malignancy or loss of tissue in a bilateral cleft lip. The lips must remain closed until the flap "takes," and then it can be detached from its blood supply. Usually, this operation is performed in children of an older age under local anesthesia, but it occasionally requires general anesthesia if the patient is young. All the problems of a closed mouth, such as the possibility of vomiting and aspiration, are encountered in addition to those associated with preservation of the flap.

Koshy JC, Ellsworth WA, Sharabi SE, et al. Bilateral cleft lip revisions: the Abbe flap. *Plast Reconstr Surg*. 2010;126(1):221–7.

C.8. What is the crucial problem of anesthesia for cleft palate? What are the unique considerations of this surgical repair?

The establishment, maintenance, and protection of the airway comprise the crucial problem of anesthesia for palate surgery. Failure to establish, maintain, and protect the airway results in tachypnea, CO_2 retention, hypoxemia, increased bleeding, hypovolemia, arrhythmia, cardiac arrest, and death. The major cause of cardiac arrest in infants and children is hypoxia.

Positioning of the patient is usually supine with table rotated 90 degrees to 180 degrees with oral RAE or reinforced endotracheal tube extending down the midline of the jaw taped to the chin. The mouth gag that is used for surgical exposure may be released intermittently to allow reperfusion of the tongue. However, each manipulation may affect the endotracheal tube. Blood that collects in the oropharynx should be carefully suctioned at the end of the procedure without disrupting the suture line. Residual blood and secretions in the oropharyngeal cavity may irritate the larynx and cause laryngospasm.

Jaffe RA, Samuels S, eds. *Anesthesiologist's Manual of Surgical Procedures*. 4th ed. Lippincott Williams & Wilkins; 2009:1417–1418.

C.9. What is laryngospasm? How would you make a diagnosis of laryngospasm?

This is defined as glottic closure resulting from a reflex constriction of the laryngeal muscles. It is much more common in pediatric anesthesia than in adults. Incidence is twice that of adults in older children and three times that of adults in younger children. Airway complications are further increased in children with upper respiratory tract infections. In the pediatric patient, the oxygen consumption is greater; thus, the consequences of laryngospasm in children may be more serious. The oxygen consumption is highest in the youngest patients.

Laryngospasm can occur during anesthesia for two reasons: first, a lack of inhibition of glottic reflexes because of central nervous system depression; and, second, increased number of stimuli—such as manipulation of the airway, secretions or blood irritating the cords, and stimulation of visceral nerve endings at an inadequate depth of anesthesia.

Bingham R, Lloyd-Thomas A, Sury M, eds. *Hatch & Sumner's Textbook of Paediatric Anesthesia*. 3rd ed. London: Hodder Arnold; 2008:288–289.

C.10. How would you manage the patient with laryngospasm?

Laryngospasm may be partial or complete. Partial spasm will be diagnosed by a characteristic stridulous noise and a mismatch between the patient's respiratory effort and

the disappointingly small movements of the reservoir bag. Methods of overcoming laryngospasm include applying positive pressure to the airway, deepening anesthesia, and administering muscle relaxants or a bolus of propofol. Recently, it was found that a bolus of propofol works extremely quickly, without the side effects of succinylcholine. The exact mechanism of action of propofol is not clear, but it could be due to increasing the depth of anesthesia or direct effect on the glottis. When there is complete laryngospasm, there will be silence with regard to air movement. The application of positive pressure may not be helpful in these circumstances and indeed may make the situation worse by forcing the false cords against the tightly closed true cords. It is much better to relax the cords before the hypoxia is severe. Succinylcholine can be given intramuscular or intravenous.

Bingham R, Lloyd-Thomas A, Sury M, eds. *Hatch & Sumner's Textbook of Paediatric Anesthesia*, 3rd ed. London: Hodder Arnold; 2008:288–289.

D. Postoperative Management

D.1. What complications of cleft lip and cleft palate surgery may be seen in the recovery room?

Complications include airway obstruction, bleeding, and hypothermia. Airway obstruction is the result of closure of the cleft structures plus some edema secondary to trauma. In case of pushback procedure with or without a pharyngeal flap, the obstruction is due to the new posterior position of the palate and the pharyngeal flap.

Combination of a closed palate, a small mandible pushing the tongue into a small pharynx, edema, blood, and the residual effects of anesthesia make postextubation airway obstruction more likely. There could also be swelling of the tongue due to mouth gag placement during surgery.

Anesthesiologist must be aware of the potential problems such as subglottic edema, flap edema, increased oral secretions, posterior displacement of tongue, mucosal swelling of hypopharynx, and overlooked throat pack.

Blood loss is not an anesthetic complication but its replacement is an anesthesiologist's responsibility, as is prevention of aspiration.

Hypothermia delays emergence and produces metabolic acidosis and respiratory and myocardial depression. The most important problem for the anesthesiologist is maintenance of the airway.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia: Mosby, Elsevier Science; 2011:831–836.

D.2. How do you protect the airway postoperatively?

Following palatoplasty, the pharynx and the nasopharynx are suctioned before extubation. Some anesthesiologists advocate that this be done with the aid of the laryngoscope to ensure removal of any mucus, blood, or clots. If suctioning is done before removing the Dingman gag, the laryngoscope may not be necessary. The infant should be as awake as possible. A long traction suture is placed through the tongue and tied loosely. Traction on the suture stimulates respiration and clears the airway. Neither an oral nor a nasal airway should be inserted unless absolutely necessary; either one could disrupt the sutures and undo all the surgical work. The traction suture is removed when the infant leaves the recovery room.

Following palate surgery, the infant is placed in prone or lateral position with the head dependent, turned to the side, and hyperextended. This position can be achieved with a jack placed under the foot of the crib or by placing a bulky bath blanket under the hips of the infant. Any blood or mucus will accumulate in the dependent cheek or roll out of the mouth.

Following cleft lip surgery, a Logan bow is frequently used to take the tension off the newly sutured lip. The infant can still be placed in the lateral position. Elbow restraints are essential, and they are placed on the infant or the child before leaving the operating room. A high-humidity atmosphere is recommended postoperatively to reduce the incidence of tracheitis, but others have failed to show any correlation between the use of humidity and the incidence of tracheitis.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia: Mosby, Elsevier Science; 2011:831–836

D.3. How would you control postoperative pain in patients following a cleft lip and a cleft palate repair?

The continuum of pain management continues through to the recovery room, the pediatric intensive care unit, or to an inpatient bed in patients with a cleft lip or a cleft palate repair. No child should be discharged from the recovery room with uncontrolled pain. Cleft palate repair is associated with the risk of postoperative airway obstruction, which may be increased with administration of opioids. Nerve blocks may be used to improve pain relief, to decrease perioperative consumption of opioids, and to favor early feeding resumption after repair.

Infraorbital nerve block can be used for pain control after a cleft lip repair. Nasopalatine and palatine nerve blocks will provide palatal hard and soft tissue anesthesia. Recently, bilateral maxillary nerve blocks using a suprazygomatic approach has been used for effective pain relief.

Opioid analgesics that can be used postoperatively are shown in Table 42.2.

Nonopioid analgesics that can be used postoperatively are shown in Table 42.3.

Lonnqvist PA, Morton NS. Paediatric day-case anaesthesia and pain control. *Curr Opin Anaesthesiol*. 2006;19:617–621.

Mesnil M, Dadure C, Captier G, et al. A new approach for peri-operative analgesia of cleft palate repair in infants: the bilateral suprazygomatic maxillary nerve block. *Paediatr Anaesth*. 2010;20(4):343–349.

Table 42.2 Opioid Analgesics for Pediatric Patients

DRUGS	DOSAGE	FORM
Fentanyl	1 μg/kg	IV
Morphine	0.05–0.1 mg/kg	IV
Meperidine	1 mg/kg	IV
Codeine	1.5 mg/kg q4h	PO: 15-mg, 30-mg, 60-mg tablets; syrup 15 mg/mL
Oxycodone	0.15 mg/kg	PO: 5-mg tablets; syrup 5 mg/mL

IV, intravenous; PO, by mouth.

Table 42.3 Nonopioid Analgesics for Pediatric Patients

DRUG	DOSAGE	FORMS AVAILABLE
Acetaminophen (Tylenol)	10–15 mg/kg PO maximum 2,600 mg/d	Tablets: 80 mg
		Syrup: 325 mg/5 mL
		Suppositories: 120, 325, 650 mg
Ibuprofen (Motrin)	10–20 mg/kg PO q6h	Tablets: 300, 400 mg
		Syrup: 100 mg/5 mL
Ketorolac (Toradol)	0.5 mg/kg IV to load (maximum dose 30 mg)	Parenteral form used intramuscularly/intravenously
	0.5 mg/kg q8h intramuscularly or intravenously (limit use to 48 hr)	

IV, intravenous; PO, by mouth.

CHAPTER 43

Congenital Heart Disease with a Cervical Mass in Infancy

Miles Dinner and Marie A. Sankaran Raval

A 1-WEEK-OLD MALE INFANT

was diagnosed shortly after birth with an interrupted aortic arch (IAA). The workup revealed the child to have a 22q11 deletion syndrome (formerly known as *DiGeorge syndrome*). An enlarging cervical mass was noted, and the child was brought to the operating room for exploration.

A. Medical Disease and Differential Diagnosis

1. What is the 22q11 deletion syndrome?
2. What are the associated cardiovascular defects in 22q11 deletion syndrome?
3. What are the endocrinologic consequences of 22q11 deletion syndrome and the attendant manifestations?
4. What are the immunologic findings in 22q11 deletion syndrome?
5. What is the differential diagnosis of cervical masses in infancy?
6. What is a cystic hygroma? What are the complications? What is the treatment?
7. What is the IAA anomaly?
8. What is the pathophysiology of the IAA syndrome?
9. How is ductal patency maintained?
10. What are the side effects of prostaglandin infusion?
11. What is the hyperoxia test?

B. Preoperative Evaluation and Preparation

1. What preoperative studies should be obtained to evaluate the neck mass?
2. How would you categorize the difficult airway in children?
3. What features of the difficult airway can be noted on physical examination?
4. How would you optimize preoperatively the ability to secure the airway in the operating room?
5. What laboratory studies are necessary before surgery?

6. What are the causes of congestive heart failure (CHF) in the infant? How would you assess this infant on your preoperative evaluation for signs of CHF?
7. How would you optimize the preoperative treatment of CHF?
8. How would you premedicate this infant?
9. When is premedication useful in infants and children?
10. Before the planned surgery, the infant is scheduled for a magnetic resonance imaging (MRI) scan. You are asked to ensure that the baby remains immobile for 20 minutes to perform the scan adequately. How would you accomplish this?

C. Intraoperative Management

1. What anesthesia equipment, circuit, and monitors would you use?
2. Describe techniques other than direct laryngoscopy that would be useful for securing the airway in this baby.
3. How would you monitor blood loss in this patient?
4. What anesthetic technique should be used in a patient who may experience severe loss of blood intraoperatively?
5. How would you induce anesthesia in this infant?
6. Intraoperatively, the surgeon must dissect the tumor in the anterior mediastinum and needs to have a quiet surgical field. How would you accomplish this in the infant?

D. Postoperative Management

1. How would you manage this patient postoperatively?

A. Medical Disease and Differential Diagnosis

A.1. What is the 22q11 deletion syndrome?

Formerly known as *DiGeorge syndrome*, this constellation of abnormalities results from an embryogenic disruption in the formation of the third and fourth aortic arches. It occurs in approximately 1 in 4,000 births. The velocardiofacial syndrome with features of facial, palatal, developmental, and cardiac abnormalities is distinct from the DiGeorge syndrome but has the same 22q11 deletion.

The common clinical features are hypocalcemia, immunodeficiency, dysmorphic facial features, palatal and velopharyngeal dysfunction, renal anomalies, and congenital heart disease (CHD). A significant number of patients with tetralogy of Fallot and IAA have a 22q11 deletion.

The DiGeorge anomaly is characterized by thymic and parathyroid aplasia or hypoplasia, cardiovascular defects, and dysmorphic facies. It arises as a consequence of a developmental defect in the embryology of the third and fourth pharyngeal pouches. It is currently thought to be caused by inadequate neural crest migration into the pharyngeal pouches, with the subsequent limitation in growth of the derivative structures. The condition arises from Mendelian disorders, teratogen exposure, or cytogenetic abnormalities. A chromosome 22q11 microdeletion is a constant finding. Depending on the extent of the thymic hypoplasia, clinical manifestations can range from little trouble with infections to severe immunodeficiency that can be corrected with cultured thymic tissue transplant, bone marrow transplant, or peripheral blood transplant.

Goldmuntz E. DiGeorge syndrome: new insights. *Clin Perinatol.* 2005; 32:963–978.

Kliegman RM, Behrman RE, Jenson HB, et al., eds. *Nelson Textbook of Pediatrics*. 18th ed. Philadelphia: Saunders, 2007:884–885.

A.2. What are the associated cardiovascular defects in 22q11 deletion syndrome?

Congenital heart defects are found in 80% of patients with this syndrome. Most patients with DiGeorge syndrome have associated anatomic cardiovascular anomalies involving the aortic arch system. The most common abnormality is tetralogy of Fallot, followed by tetralogy of Fallot with pulmonary atresia, isolated ventricular septal defect (VSD), IAA, and truncus arteriosus. These defects arise during the crucial developmental stages of the truncoconal parts of the heart from the pharyngeal pouch derivatives. Cardiac MRIs are invaluable in defining the aortic arch anatomy in detail

Momma K. Cardiovascular anomalies associated with chromosome 22q11.2 deletion syndrome. *Am J Cardiol*. 2010;105:1617–1624.

A.3. What are the endocrinologic consequences of 22q11 deletion syndrome and the attendant manifestations?

Thymic aplasia occurs in approximately 60% of patients with the 22q11 syndrome. These patients fail to make parathyroid hormone, or they are severely deficient in its production, leading to hypocalcemia. Hypocalcemia in the neonate is often difficult to detect clinically but it can lead to irritability; jitteriness; twitching; or frank seizure activity, failure to thrive, tachycardia, and hypotension. Stridor, syncope, and carpopedal spasm may occur. Trousseau sign (carpopedal spasm elicited by an inflated blood pressure cuff) and Chvostek sign (twitching of facial muscles after tapping the facial nerve) can be seen. Growth hormone and thyroid hormone deficiency have been reported.

Brauner R, Le Harivel De Gonneville A, Kindermans C, et al. Parathyroid function and growth in 22q11.2 deletion syndrome. *J Pediatr*. 2003;142:504–508.

Sperling MD, Mark A, eds. *Pediatric Endocrinology*. 3rd ed. Philadelphia: Saunders; 2008:690–696.

A.4. What are the immunologic findings in 22q11 deletion syndrome?

Patients with the 22q11 deletion syndrome demonstrate marked variability in the degree of involvement of the immune system. Total lymphocyte counts, percentage of T cells, and T-lymphocyte function ranges from normal to severely depressed. The most consistent abnormality is a decrease in total T cells, which is seen in approximately 75% to 80% of these patients. Approximately 1% of patients have thymic aplasia requiring transplant and 20% have no evidence of reduced T cells. Spontaneous resolution of immunodeficiency occurs in some patients, but progressive loss of function can be seen in others. Patients with the partial DiGeorge anomaly can be immunized and generate good antibody responses; therefore, humoral immunity is often intact, as is functional cellular immunity.

Markert ML, Alexieff MJ, Li J, et al. Complete DiGeorge syndrome: development of rash, lymphadenopathy, and oligoclonal T cells in 5 cases. *J Allergy Clin Immunol*. 2004;113:734–741.

Sullivan, KE. Chromosome 22q11.2 deletion syndrome: DiGeorge syndrome/velocardiofacial syndrome. *Immunol Allergy Clin North Am*. 2008:28:353–366.

A.5. What is the differential diagnosis of cervical masses in infancy?

Neck masses can originate from a congenital anatomic anomaly, neoplasm, or infection. In the first category are branchial cysts, thyroglossal duct cysts, and failed thymic descent. Branchial cysts arise in the embryo from the thymic stalk or the pharyngeal pouch. They may be present at birth or arise later. They lie beneath the sternomastoid muscle and may bulge out from the anterior border. They can become infected and thereby enlarge with pus. When this occurs, the airway or upper esophagus may be compressed. Thyroglossal duct cysts are spherical, midline masses that may extend back to the base of the tongue and may represent all of the thyroid tissue that the baby has. The thymus gland arises high in the neck and must descend in the embryo to the anterior mediastinum. If this caudad movement becomes arrested, the thymus can appear as a soft, compressible mass along the anterior border of the sternocleidomastoid muscle.

Infectious masses can be due to tuberculosis, Kawasaki disease, Epstein-Barr viral infection, Ludwig angina, and catscratch disease. Neoplastic masses in the cervical region can be teratomas, hemangiomas, neurofibromas, lymphomas, goiters, or cystic hygromas. Teratomas are firm, midline masses arising adjacent to the thyroid isthmus. Hemangiomas may be extensive and compress vital structures. Neurofibromas may arise individually or as a consequence of neurofibromatosis (von Recklinghausen syndrome) and they can be very large. A goiter represents an enlarged thyroid gland that may be hypothyroid, hyperthyroid, or euthyroid.

Long SS. *Principles and Practice of Pediatric Infectious Diseases*. 2nd ed. Orlando, FL: WB Saunders; 2003:170–171.

Ungkamont K, Yellon RF, Weissman JL. Head and neck space infections in infants and children. *Otolaryngol Head Neck Surg*. 1995;112:375–382.

A.6. What is a cystic hygroma? What are the complications? What is the treatment?

Cystic hygroma is a developmental malformation of the lymphatic system found most often in the posterior triangle of the neck and axilla of children. They are divided into suprahyoid and subhyoid masses. They are compressible masses that are most often found in infants younger than 1 year and they intermittently enlarge. Suprahyoid masses can be extremely difficult to manage because of the obstructive symptoms and feeding difficulties, and they may become infected, producing rapid compromise of breathing.

Complete surgical removal of these masses is often impossible, and repeat debulking is sometimes the only treatment. Facial paresis may be a consequence of resection. The mortality of obstructing cystic hygroma diagnosed prenatally exceeds 20% following delivery. Intubation of the neonate during delivery under uninterrupted maternal–fetal circulation has been performed to prevent the fatal consequences of immediate postpartum airway obstruction. Bleomycin or derivatives of *Streptococcus pyogenes* have been used as a sclerosing agents with favorable results.

Burezq H, Williams B, Chitte SA. Management of cystic hygromas: 30 year experience. *J Craniofac Surg*. 2006;17:815–818.

Descamps P, Jourdain O, Paillet C, et al. Etiology, prognosis and management of nuchal cystic hygroma: 25 new cases and literature review. *Eur J Obstet Gynecol Reprod Biol*. 1997;71:3–10.

Townsend CM Jr., Beauchamp RD, Evers BM, et al., eds. *Sabiston Textbook of Surgery*. 18th ed. Philadelphia: Saunders; 2008:2052–2053.

A.7. What is the IAA anomaly?

IAA is a group of three anatomic abnormalities in which the aorta has a complete atresia at a site somewhere along the arch. If untreated, it is uniformly lethal within 1 week of life as a consequence of closure of the ductus arteriosus. In type A, which accounts for 43%, the aorta is interrupted between the left subclavian artery and the aortic isthmus. Type B, the most common (53%), has the lack of continuity between the left carotid and the left subclavian arteries. The defect in type C is distal to the brachiocephalic artery and is the least common of three types. A VSD is frequently associated with 22q11.2 syndrome. Approximately 50% of patients with IAA have DiGeorge syndrome. IAA can also coexist with a single ventricle and atrioventricular canal.

Brown JW, Ruzmetov M, Okada Y, et al. Outcomes in patients with interrupted aortic arch and associated anomalies: a 20-year experience. *Eur J Cardiothorac Surg.* 2006;29:666–673.

Goldmunte E, Clark BJ, Mitchell LE, et al. Frequency of 22q11 deletions in patients with conotruncal defects. *J Am Coll Cardiol.* 1998;32:492–498.

Momma K. Cardiovascular anomalies associated with chromosome 22q11.2 deletion syndrome. *Am J Cardiol.* 2010;105:1617–1624.

A.8. What is the pathophysiology of the IAA syndrome?

Because of the discontinuity between the descending aorta and the arch, blood flow to the descending aorta cannot occur unless a patent ductus arteriosus exists. Pulse oximetry will reveal normal saturation in the right arm, with a decreased saturation in the lower extremities. If the ductus is inadequate to provide perfusion to the lower body because of its closure, severe metabolic acidosis, CHF, renal insufficiency, and shock may develop. With a VSD, most of the cardiac output will be directed into the pulmonary vascular bed as the ductus closes. Ductal patency can be maintained with prostaglandins. Symptoms of ductal closure include tachypnea, lethargy, and poor feeding. Two-dimensional echocardiography is diagnostic.

Kliegman RM, Behrman RE, Jenson HB, et al., eds. *Nelson Textbook of Pediatrics*. 18th ed. Philadelphia: Saunders; 2007:1900–1903.

A.9. How is ductal patency maintained?

The ductus arteriosus is kept open by the infusion of prostaglandin E_1 (PGE_1). Both PGE_1 and prostaglandin E_2 are produced endogenously in the ductus, metabolized in the lungs, and achieve high levels in the fetus relative to adults. Among the endogenous prostaglandins, prostaglandin E_2 is the most important. Postnatally, the levels fall associated with increased metabolism resulting from the increase in pulmonary blood flow. An infusion of prostaglandin will delay the natural closure of the ductus and improve systemic arterial oxygenation. Less acidosis will also be seen in arterial blood gases compared to those obtained before PGE_1 infusion administration. In the case of an IAA, circulation to the lower body is totally dependent on the patency of the ductus, and, therefore, continual infusion of PGE_1 is critical to keep the infant alive. The infusion is titrated at a rate of 0.05 to 0.1 μg/kg/min. Because of its relatively long half-life, discontinuation of the drip will not acutely cause ductal closure in the event of inadvertent stoppage.

Freed MD, Heymann MA, Lewis AB, et al. Prostaglandin E_1 in infants with ductus arteriosus-dependent congenital heart disease. *Circulation*. 1981;64:889–905.

Hermes-DeSantis ER, Clyman RI. Patent ductus arteriosus: pathophysiology and management. *J Perinatol*. 2006;26(suppl 1):S14–S18.

Kliegman RM, Behrman RE, Jenson HB, et al., eds. *Nelson Textbook of Pediatrics*. 18th ed. Philadelphia: Saunders; 2007:2956.

A.10. What are the side effects of prostaglandin infusion?

Prostaglandin infusion has a variety of side effects ranging from fever to hypotension, seizure-like activity, flushing, and edema. Platelet aggregation may be reduced. Apnea and bradycardia can also occur, which may require prophylactic intubation and mechanical ventilation. A separate intravenous line must be used.

Kliegman RM, Behrman RE, Jenson HB, et al., eds. *Nelson Textbook of Pediatrics*. 18th ed. Philadelphia: Saunders; 2007:2956.

A.11. What is the hyperoxia test?

This test is performed to distinguish pulmonary and cardiac causes of cyanosis. To perform the test, the patient is first placed on 100% oxygen for 10 minutes. A pre-ductal arterial blood gas is then taken from the patient's right arm. Supplemental oxygen in patients with pulmonary disease significantly augments systemic oxygenation, which is not the case in cyanotic congenital heart defects. Of course, in severe pulmonary conditions, there may be a failure to raise the oxygen tension meaningfully but the chest radiograph would be valuable in affirming the diagnosis of lung pathology. Similarly, in some congenital heart lesions with mixing such as truncus arteriosus, the supplemental o_2 decreases pulmonary vascular resistance resulting in an increase in oxygen tension but rarely more than 150 mm Hg.

Keane JF, Locke JE, Fyler DC, eds. *Nadas' Pediatric Cardiology*. 2nd ed. Philadelphia: Saunders; 2006: 141–142.

B. Preoperative Evaluation and Preparation

B.1. What preoperative studies should be obtained to evaluate the neck mass?

Cervical masses have a variable nature, invasiveness, and potential for airway compression. Thus, MRI studies and a sonogram should be obtained before surgery to better define the nature of the cystic hygroma and highlight the region of airway compression. These cysts are known to invade the anterior mediastinum and can, therefore, cause extrinsic distortion of the lower airway anywhere from the cricoid ring to the carina. Cystic fluid can be aspirated under sonography to reduce the size of the mass and potentially relieve compressive symptoms. On rare occasions, there may be ingrowth of the pericardium and displacement of the lung. For suprahyoid masses, radiologic studies will define the scope of laryngeal compression and retropharyngeal involvement, which will obviously affect the ability to intubate the trachea. A flexible neonatal bronchoscopic examination can define extrinsic compressive deformations of the airway.

B.2. How would you categorize the difficult airway in children?

Children with difficult airways can be grouped into four main groups. The first group includes children who have congenital anomalies affecting the airway such as vascular rings, laryngomalacia, micrognathia, and neurofibromatosis. Second would be children with an acute acquired obstruction such as injury or foreign body. The third group includes infectious causes such as retropharyngeal abscess, croup, diphtheria, and peritonsillar abscess. In the last group are those children who prove to be difficult to visualize on intubation and who do not have known congenital abnormalities.

Hall SC. The child with a difficult airway: recognition and management. *ASA Annual Meeting Refresher Course Lectures*. Park Ridge, IL: American Society of Anesthesiologists; 2006:412.

B.3. What features of the difficult airway can be noted on physical examination?

Starting at the mouth and working caudally, we can examine a host of physical features that can challenge the clinician. Many anatomic abnormalities can be discerned before direct laryngoscopy. Conditions that result in a constricted oral opening, such as scleroderma, epidermolysis bullosa, burn cicatrization, or congenital microstomia prevent insertion of the laryngoscope. A small lower jaw and maxillary protrusion often accompany the anterior larynx, making laryngeal inlet exposure during laryngoscopy impossible. This is seen in children with syndromes such as Pierre Robin, Apert syndrome, Crouzon syndrome, Treacher Collins syndrome, and many other craniofacial syndromes.

Macroglossia as a consequence of certain metabolic storage diseases, cystic abnormalities, and hamartomatous tumors of the tongue (Goltz syndrome) can make effective laryngoscopy impossible.

Temporomandibular ankylosis, as seen in patients with juvenile rheumatoid arthritis and other rheumatic processes, may prevent mouth opening. A narrow, high-arched palate may suggest a problematic intubation. Neck extension problems may accompany some neuromuscular disorders, trauma, arthritis, or Goldenhar syndrome.

Berry FA, ed. *Anesthetic Management of Difficult and Routine Pediatric Patients*. New York: Churchill Livingstone; 1986:167.

Wetmore RF, Muntz HR, McGill TJ. *Pediatric Otolaryngology: Principles and Practical Pathways*. New York: Thieme Medical; 2000:775.

B.4. How would you optimize preoperatively the ability to secure the airway in the operating room?

Because of the risk inherent in inducing anesthesia in this infant, plan for a fiberoptic laryngoscopy. The infant bronchoscope is of such small diameter that it does not have a suction port, and visualization is especially impaired because of secretions. An antisialagogue is a must to permit proper anatomic recognition through the fiberoptic scope. Glycopyrrolate (0.01 mg per kg) given half an hour before anesthesia will limit secretions without the excessive tachycardia that may occur with atropine. In this infant with cardiac compromise, any unnecessary stress on the heart should be avoided. An appropriate laryngeal mask airway (LMA), in this case a no.1, should be readied, as should equipment trays for emergency cricothyrotomy. Adjunctive devices such as a rigid infant bronchoscope with video imaging can be tremendously useful should fiberoptic or classical laryngoscopy prove too difficult. An appropriate-sized

rigid scope can serve to visualize the laryngeal inlet and hold the endotracheal tube as an introducing stylet to facilitate intubation.

An updated report by the American Society of Anesthesiologists Task Force on Management of Difficult Airway. Practice guidelines for management of the difficult airway. *Anesthesiology*. 2003;98:1269–1277.

DeLeo A, Dimmitt P. Pediatric upper airway endoscopy. *ORL Head Neck Nurs*. 2005;23:29–30.

B.5. What laboratory studies are necessary before surgery?

Because of the strong association of 22q11 deletion syndrome with hypocalcemia, serum calcium should be measured. In addition, because of the inherent dysphagia with a cystic hygroma, the infant will not have been feeding. To ensure that adequate parenteral nutrition and hydration were provided, serum glucose and sodium levels should be noted. Because of the potential for severe metabolic acidosis secondary to underperfusion of the lower body through the interrupted descending aorta, a serum pH and bicarbonate concentrations must be obtained. A $Paco_2$ level will indicate the adequacy of ventilation in the face of a potentially obstructing mass, and a baseline Pao_2 level will serve as a guideline to the infant's degree of CHF, pulmonary insufficiency, and central shunting.

Because the surgery can be extensive, with a significant loss of blood, a baseline complete blood count with hematocrit should be obtained. In addition, the prothrombin time and partial thromboplastin time should be obtained before surgery of this magnitude because of the possibility of baseline immaturity in coagulation factor production and the inherent bleeding potential from the large dissection that will be done. Specific gravity of the urine will suggest the diagnosis of dehydration, although urinary concentrating ability does not mature until the infant is 3 months of age. A chest radiograph will define the state of the lungs and indicate whether there is tracheal deviation.

B.6. What are the causes of congestive heart failure (CHF) in the infant? How would you assess this infant on your preoperative evaluation for signs of CHF?

The causes of CHF can be divided into five major areas:

- Cardiac rhythm disturbances (heart block and supraventricular tachycardia)
- Volume overload (anemia, sepsis, and VSD)
- Systolic ventricular dysfunction (myocarditis, malnutrition, and dilated cardiomyopathy)
- Pressure overload (aortic stenosis and coarctation)
- Diastolic ventricular dysfunction (pericardial tamponade and restrictive cardiomyopathy)

CHF occurs either in response to an excessive volume or pressure load or as a consequence of myocardial muscle impairment. Volume overload is due to factors causing a large increase in cardiac output (e.g., large VSD or ductus arteriosus). In these circumstances, there must be a sufficiently large left-to-right shunt to cause a severe strain on the heart. In the normal newborn, these lesions do not usually produce heart failure until 1 to 2 months of age because it takes longer than usual for the pulmonary vascular resistance to fall. The elevated pulmonary vascular resistance protects the left ventricle from the stress of overcirculation. This is not true in premature infants who do not manifest the same degree of pulmonary arteriolar constriction. Therefore, they are susceptible to large left-to-right shunts early and show CHF more easily.

Regurgitant valvular lesions can lead to CHF. In complex CHD, such as truncus arteriosus or tricuspid atresia with transposition, the additional stress of hypoxemia or univentricular overload may herald the early onset of CHF. Large arteriovenous malformations may occur intracranially and cause CHF. Excessive pressure loads are seen in obstruction to cardiac output from aortic stenosis, aortic coarctation, and aortic interruption. In the immediate newborn period, right-sided CHF is seen with greater frequency because of severe pulmonary hypertension. Pulmonary hypertension has many causes: intrinsic lung parenchymal insufficiency or pathology, as in diaphragmatic hernia, meconium aspiration or hyaline membrane disease, chronic hypoxemia, hypervolemia, and polycythemia.

Primary myocardial failure is unusual in the newborn; it occurs with endocardial fibroelastosis and anomalous coronary circulation. However, the myocardium in the infant is susceptible to depression from metabolic derangements such as hypoglycemia, hypocalcemia, or birth asphyxia. Certainly, severe anemia with the associated decrease in systemic and myocardial oxygen supply forces an increase in myocardial work that can lead to CHF.

Infants are different from adults in their manifestations of CHF. Because of possible coexisting lung disease in many premature infants, signs of cardiac dilation may be absent because of the decreased systemic venous return from elevated intrathoracic pressure. Although immature, the carotid baroreceptors still initiate an increase in sympathetic outflow in response to reduced perfusion. The increased α-adrenergic stimulation impairs blood flow to the systemic arteriolar beds, resulting in cold, underperfused extremities, and diminished splanchnic perfusion. Fatigue, loss of appetite, and failure to thrive follow. Tachycardia from β-receptor stimulation occurs. Generalized sweating results from sympathetic cholinergic fiber stimulation. Extracellular water increases because of decreased renal excretion of sodium from a lowered glomerular filtration rate. Peripheral pitting edema is much less common in infants than older children and adults. The venous system in infants is extremely distensible and, therefore, raised right atrial pressure may not show large jugular venous engorgement. The most prominent manifestation of CHF in the infant is tachypnea. Because pulmonary venous pressure is elevated from left ventricular failure, the lung compliance falls because of the augmented interstitial fluid. Breathing becomes rapid and shallow and the resultant increase in oxygen requirement causes a cyclic dependency to maintain both tachycardia and tachypnea. Subcostal retractions are seen because of the increase in respiratory effort.

Infants have a greater lymphatic drainage capacity than adults and, therefore, can clear interstitial accumulations more readily. Therefore, rales are not as frequent a manifestation of CHF in infants as in adults. The bronchial mucosa may be swollen because of the engorgement of the bronchial venous system. The lumen of the airway is narrowed, resulting in wheezing that is often seen in infantile CHF. Hepatomegaly is a cardinal sign of right ventricular failure in infants.

Kliegman RM, Behrman RE, Jenson HB, et al., eds. *Nelson Textbook of Pediatrics*. 18th ed. Philadelphia: Saunders; 2007:1976–1981.

B.7. How would you optimize the preoperative treatment of CHF?

The typical manifestations of CHF in infants, namely tachycardia, tachypnea, subcostal retractions, and rhonchi, are also cardinal signs of pulmonary infection in this age group. They are difficult to distinguish. Often, they coexist and treatment must address both conditions. In this patient, the structural abnormality, the IAA, needs surgical correction; nevertheless, correction must be deferred until the neck mass is resected. In this infant, the CHF is caused by pressure overload from the IAA and the hypocalcemia is due to parathyroid hormone insufficiency. Calcium must be

normalized by intravenous infusion. If glucose is low, as would be expected in undernourishment, glycogen depletion from the stress of illness, or increased utilization, it should be supplemented by slow intravenous administration. Myocardial work is compromised by the presence of metabolic acidosis, which occurs as a consequence of the increased lactic acid production during anaerobic metabolism. The pH should be normalized with sodium bicarbonate. Because of the attendant sodium load, tromethamine may be an alternative.

Myocardial function should be optimized with digitalis in most infants with CHF, although in the IAA syndrome, there may be decreased renal perfusion. As a consequence, the digoxin levels may rise and toxicity may occur. Catecholamine (e.g., dopamine or dobutamine) should be infused to boost contractility. Pulmonary symptoms should be treated with antibiotics and positive pressure ventilation with oxygen carefully adjusted to arterial blood gas measurements. Intubation and mechanical ventilation may be necessary in many infants with CHF. Diuresis with furosemide will promote restoration of pulmonary compliance by decreasing lung water in conjunction with fluid restriction.

Balaguru D, Artman M, Auslander M. Management of heart failure in children. *Curr Probl Pediatr*. 2000;30:5–30.

McMillan JA, Feigin RD, DeAngelis C, et al., eds. *Oski's Pediatrics: Principles and Practice*. 4th ed. Philadelphia, Lippincott Williams & Wilkins; 2006:357.

B.8. How would you premedicate this infant?

Infants younger than 2 years do not routinely require preoperative anxiolytics or narcotics. Premedicants such as midazolam have no place in this scenario. An infant with a compromised airway and circulation cannot tolerate any degree of respiratory depression. Therefore, no sedatives should be given at all. As mentioned, because a fiberoptic intubation is planned, glycopyrrolate should be given for its antisecretory activity.

B.9. When is premedication useful in infants and children?

Patients with dynamically responsive cyanotic CHD (e.g., tetralogy of Fallot) benefit from premedication before coming to the operating room. In these children, the inherent anxiety of transfer to unfamiliar surroundings, change in temperature, and parental separation may trigger infundibular spasm and reduce pulmonary blood flow, thereby leading to a blue spell. Acute hypoxemia is not an optimal state in which to initiate an anesthetic induction. Therefore, sedation with oral midazolam or rectal pentobarbital is useful to allay the child's impending state of panic and reduce the risk for provoking a hypoxemic spell. Of course, premedication is always helpful to make the overall experience of the operating room less imposing to the young child. In producing variable degrees of amnesia and reducing the potential for physical agitation, premedication offers a real benefit for children intensely frightened of the operating room.

B.10. Before the planned surgery, the infant is scheduled for a magnetic resonance imaging (MRI) scan. You are asked to ensure that the baby remains immobile for 20 minutes to perform the scan adequately. How would you accomplish this?

Given this infant's extreme risk for complete airway occlusion, there is no safe method other than endotracheal intubation, which will guarantee immobility on demand and ensure a patent airway. The routine method of sedating an infant for an MRI scan

(i.e. chloral hydrate, oral midazolam) should not be used here. Establishing an airway emergently in this infant may be impossible even with a LMA, and, therefore, sedation can proceed only after the trachea is intubated. Section C.2 details fiberoptic intubation in infants. If the infant has demonstrated a postprandial sleep cycle and can take oral fluids, it may be well worth the attempt at an MRI by using nothing at all except the inherent feeling of wellness from a full stomach.

C. Intraoperative Management

C.1. What anesthesia equipment, circuit, and monitors would you use?

Because of the depressed cellular immunity, this patient is susceptible to infection. Therefore, particularly strict attention must be paid to sterile technique during line placement and instrumentation of the patient. The anesthesiologist must wear gowns and gloves to protect the infant. Sterility of the disposable circle system, mask, endotracheal tube, fiberoptic bronchoscope, and laryngoscope should be ensured. Routine monitors for all surgery on infants include a precordial stethoscope, rectal temperature probe, electrocardiogram, blood pressure, capnograph, and spirometer. Multiple pulse oximeters should be used to offer flexibility in the event of dysfunction. In this case, the IAA prevents saturation data from the lower body and left arm. End-tidal expired gas concentrations should be recorded for anesthetic gases, nitrogen, and oxygen. Accurate capnography in small infants may be hampered by side-arm gas sampling resulting from the relatively high gas flows relative to the expired gas flow from the infant.

In this procedure, an arterial line should be inserted in the right radial site because the IAA will not allow for pressure determination on the left side. Because of the potential for significant blood loss, a central line should be placed through either the femoral vein or subclavian vein if possible. Keep in mind the distorted anatomy and the potential for difficulty in cannulation with the subclavian site. If the subclavian site is elected, before proceeding with this complicated case, a chest radiograph should be obtained to document the absence of a pneumothorax and good line position. The femoral vein may be chosen as an alternative site. Catheter length is important, and it is easy in an infant to inadvertently place the central line across the tricuspid valve, in which case misleading values of the right ventricular pressure would be obtained. Remember, in setting the transducer height that small variances in the alignment of the zero point can result in relatively large central venous pressure (CVP) value discrepancies. Therefore, the transducer should be placed with great care to approximate the right atrial level and be moved accordingly as the table height is changed.

Cerebral oximetry, described nearly 30 years ago, may be a useful intraoperative monitor to detect intraoperative ischemic events and guide intervention.

Schreiber C, Eicken A, Vogt M, et al. Repair of interrupted aortic arch: results after more than 20 years. *Ann Thorac Cardiovasc Surg*. 2000;70:1896–1899.

Rosen DA, Tobias JD. Cerebral oximetry using near-infrared spectroscopy aids in the diagnosis of interrupted aortic arch. *J Intensive Care Med*. 2008;23:335–337.

C.2. Describe techniques other than direct laryngoscopy that would be useful for securing the airway in this baby.

It is highly unlikely that laryngeal visualization could be accomplished in this infant with direct visualization. On the computed tomography scan, the mass is seen to elevate the tongue and deviate the larynx to the side. Because of this limitation in direct visualization, the clinician should be well acquainted with alternative methods

before emergently instituting them. The following techniques can be useful when laryngoscopy cannot be accomplished easily.

Infant video laryngoscope

This relatively new device allows for excellent glottic visualization and facilitation of intubation and may provide a better visualization than conventional laryngoscopy in some patients.

Intubation through an LMA

Securing the airway with an LMA and then using this as a guide for insertion of a fiberoptic-guided endotracheal tube.

Retrograde cricothyroid wire

Although technically difficult, the retrograde cricothyroid wire technique can be successful and is best for oral intubation. A guidewire is inserted through a large-gauge needle used to puncture the cricothyroid membrane and is threaded cephalad to be retrieved out through the mouth. This wire then serves as a stent for placement of the endotracheal tube.

Blind nasal intubation

Although very successful in the adult patient, the blind nasal intubation technique can be difficult in infants or small children. Certainly, performing an awake, sedated intubation in this manner mandates giving adequate topical anesthesia to a less than cooperative infant. In addition, the smaller endotracheal tubes used in pediatrics are far more compliant than others, especially when warmed with nasopharyngeal respiratory gases, which makes it difficult to maintain the anterior curve on the tube to enter the larynx. Styletted nasal tubes should be used only by clinicians skilled in this specialized technique.

Nasal intubation with laryngoscope and Magill forceps

If the larynx cannot be visualized by laryngoscopy, an anesthetized, spontaneously breathing nasal intubation with laryngoscopic assistance can be carried out in some patients. In this case, great care is taken to ensure that the patient maintains adequate ventilatory exchange during the inhalational induction. Halothane or sevoflurane is initiated because either is less pungent and more easily tolerated than the other halogenated ethers, and the anesthesiologist should be ever mindful that total obstruction is possible in some of these infants because of their airway abnormalities. If spontaneous breathing can be maintained, the intubation should be attempted after a surgical plane of anesthesia is achieved. The laryngoscope is used to visualize the epiglottis, and the tip of the endotracheal tube is aligned with the help of a Magill forceps and then advanced in the subepiglottic region. Capnographic monitoring during this maneuver can help verify the direction of the endotracheal tube tip.

Fiberoptic intubation

Fiberoptic intubation is most successful when carried out as the initial maneuver. It may be impossible to use after several unsuccessful attempts with conventional laryngoscopy because the upper airway is then often traumatized and hypersecretory. Fiberoptic technology is still not widely disseminated to the infant population. Most centers do not have the smallest, "ultrathin" bronchoscopes, which come as small as 2.2 mm in diameter. Limitations are found in their use because of the size and lack of a suction port. The endotracheal tube requires good lubrication before threading over the scope.

In older patients, three specialized fiberoptic methods are available that may be useful in intubating difficult infants. First, the clinician can pass a guidewire through

the suction port of the larger instrument to serve as a stylet for the endotracheal tube. Second, the scope can be used to visualize and guide a nasal endotracheal tube inserted into the opposite nostril. Finally, a 4.5-mm tube can be placed at the laryngeal orifice to be used as a stent for inserting a small guidewire, which can in turn be used to place a smaller endotracheal tube.

Transtracheal jet ventilation can be used when applicable. In this technique, a 16-gauge intravenous catheter is placed through the cricothyroid membrane and jet ventilation with 100% oxygen is provided. A second intravenous catheter is placed through the cricothyroid membrane and a guidewire (0.021 in. diameter J-tip) is introduced with cephalad angulation. Jet ventilation continues as the guidewire is threaded through the nose and connected to the working part of a fiberoptic scope. The scope is then advanced through the laryngeal inlet, and a tube is threaded over the scope when the guidewire is removed. Sedation can be provided with a remifentanil drip (0.1 to 0.2 μg/kg/min). Of course, safety is the foremost consideration in any technique for inserting an artificial airway. If the anesthesiologist cannot perform a cricothyrotomy, personnel capable of an accurate and quick cricothyrotomy should be on hand in case there is a life-threatening loss of airway control. In an emergency cricothyrotomy, a longitudinal incision is made in the skin and fascia above the cricothyroid membrane, after which the cricothyroid membrane is punctured and entered with a small endotracheal tube. Another technique uses a 14-gauge angiocatheter, which is inserted into the cricothyroid membrane. Intratracheal location is verified by the loss of resistance with an attached syringe and the aspiration of air. The catheter is attached to a 3-mL syringe (without plunger), which is then connected to the Y-piece of the anesthesia circuit by an adapter from a 7.0-mm internal diameter endotracheal tube.

Auden SM. Additional techniques for managing the difficult pediatric airway. *Anesth Analg.* 2000;90:878–880.

Hall SC. The child with a difficult airway, recognition and management. *ASA Annual Meeting Refresher Course Lectures.* Park Ridge, IL: American Society of Anesthesiologists; 2006:412.

Jagannathan N, Wong DT. Successful tracheal intubation through an intubating laryngeal airway in pediatric patients with airway hemorrhage. *J Emerg Med.* 2010 (epub ahead of print).

C.3. How would you monitor blood loss in this patient?

In many of these procedures, blood loss can be significant, exceeding the patient's calculated blood volume. Often, much of this loss is not measurable because blood is either lost under the drapes or irrigated away. Certainly, meticulous weighing of sponges and observation of suction canisters are important, but blood loss can be continuous from the time of skin incision and may be seemingly relentless for an inexperienced clinician. Absolute changes in the CVP are a relative guide to the volume in the central compartment, but no one isolated value correlates with a known blood volume. A falling CVP in association with a downward trend in blood pressure during periods of surgical intervention known to produce significant bleeding should be treated aggressively with brisk transfusion. If blood loss is allowed to continue, severe hypotension can rapidly ensue.

C.4. What anesthetic technique should be used in a patient who may experience severe loss of blood intraoperatively?

Blood loss should be replaced milliliter for milliliter to prevent falling behind in volume. It is wise to choose an anesthetic technique that produces a relatively stable

blood pressure throughout the surgery, so that new downward trends in blood pressure can be attributable to blood loss and not to pharmacologic action. For instance, if a steady level of desflurane or sevoflurane is given at 1.25 minimal alveolar concentration (MAC) with a resultant mean arterial pressure (MAP) 15% lower than awake, further dips in MAP during surgical intervention can be taken as intravascular volume depletion secondary to bleeding and replaced accordingly. This interpretation would be obscured if there were frequent anesthetic interventions associated with MAP changes, such as intermittent narcotization, relaxant titration, or up and down titration of hypotension-inducing agents.

An important clue to the blood volume loss of the patient is the blood pressure at a MAC of anesthesia. If a stable pressure is established at a given MAC of inhalational agent, a lower than expected blood pressure at this MAC is almost always indicative of hypovolemia and, therefore, calls for fluid or blood replacement. Frequent hematocrit determinations drawn with the arterial blood gases are important. Remember, it is most unusual in an otherwise healthy infant to produce hypotension with intravascular overload.

C.5. How would you induce anesthesia in this infant?

After securing the airway and checking for bilateral breath sounds, narcotic titration with fentanyl should be given in repeated doses of 2 μg per kg. Remember, this infant may behave sensitively to any anesthetic agent because of the cardiovascular anomalies. Therefore, beat-to-beat monitoring of the blood pressure with an arterial line, as the fentanyl is administered, ensures against inadvertent drops in pressure. Because this patient is not going to be extubated, fentanyl can be given in the range of up to 50 μg per kg or higher to allow for dense analgesia. Because this will be a long procedure, cisatracurium or a longer acting relaxant such as pancuronium can be administered. If tolerated, small concentrations of approximately 0.5% to 4% desflurane or sevoflurane 0.25% to 1.5% can be administered to synergize with the narcotic and assist with amnesia and unconsciousness. The prostaglandin infusion should be maintained throughout the entire surgery.

C.6. Intraoperatively, the surgeon must dissect the tumor in the anterior mediastinum and needs to have a quiet surgical field. How would you accomplish this in the infant?

Double-lumen tubes are not used in the neonatal age group because of the exceedingly small lumen and the technical difficulties of securing both lungs. Instead, a single-lumen endotracheal tube can be advanced to the right or left mainstem bronchus to allow for one-lung ventilation. This may be fraught with consequences in this infant with IAA, but it can still be attempted. Keep in mind that hypoxic pulmonary vasoconstriction may not occur readily in the neonate and excessive shunting may be in evidence. In addition, having an infant on one-lung ventilation may lead to an elevated $Paco_2$ from pulmonary insufficiency. During thoracotomies in infants for pulmonary banding or Blalock–Taussig shunts, it is not uncommon to see extremely elevated $Paco_2$ values from retraction of the lung, especially the right side, which has almost 60% of the total lung surface area.

Engum SA. Minimal access thoracic surgery in the pediatric population. *Semin Pediatr Surg.* 2007;16:14–26.

Lew YS. Pediatric one lung anesthesia by selective bronchial intubation. *Singapore Med J.* 2000;51:398–400.

McGahren ED, Kern DA, Rodgers BM. Anesthetic technique for pediatric thoracoscopy. *Ann Thorac Surg.* 1995;60:927–930.

D. Postoperative Management

D.1. How would you manage this patient postoperatively?

This procedure, involving extensive dissection around the neck and upper thorax, warrants that the patient stay intubated or have a tracheostomy placed. A tremendous amount of upper airway and neck edema will surely ensue, which would make extubation life threatening. To facilitate care over the next day, the patient should be well narcotized and paralyzed if necessary to coordinate effective mechanical ventilation. Artificial ventilation and oxygen supplementation should be titrated to arterial blood gas determinations. In addition, the prostaglandin drip must be continued to ensure ductal patency. Generous narcotic supplementation will ensure that the pulmonary vascular resistance stays in a state of relative quiescence. If an endotracheal tube is maintained, fiberoptic visualization of the laryngeal inlet after 24 hours will enable a more educated decision on the suitability of extubation. Anatomic airway factors aside, the IAA and associated CHF will make extubation of this baby more challenging. Assuming all other factors are under control, the following ventilatory parameters should be met before extubation: normal arterial blood gases with satisfactory oxygenation of 28% oxygen, spontaneous tidal volume greater than 5 mL per kg, and inspiratory force greater than 12 cm H_2O. One should always be on the alert for airway obstruction and ready to intercede with reintubation or tracheostomy if prompt deterioration occurs.

CHAPTER 44

Patent Ductus Arteriosus and Prematurity

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A 2-WEEK-OLD MALE INFANT weighing 900 g was scheduled for ligation of patent ductus arteriosus (PDA). He was born at 27 weeks' gestation as part of a triplet pregnancy complicated by preterm labor. Immediately after delivery, he was intubated because of respiratory distress. He was given indomethacin prophylactically because of his prematurity and presumed PDA. A transthoracic echocardiogram (TTE) confirmed the patency of the ductus arteriosus and demonstrated its closure after one course of indomethacin. His respiratory function was gradually improving with ventilatory support until 2 weeks later when his oxygenation and ventilation suddenly worsened. A murmur was heard over his chest. A repeat TTE demonstrated left-to-right shunting through the ductus arteriosus. Another course of indomethacin was administered, but the ductus remained patent. His blood pressure was 50/20 mm Hg; heart rate, 165 beats per minute. The laboratory data were as follows: white blood cell (WBC) count, 17,000 per mm^3; hemoglobin, 11 g per dL; hematocrit, 34%; urine specific gravity, 1.005; protein, 1 +; sugar, 1 +; serum calcium, 6.0 mg per dL; blood glucose, 60 mg per dL; arterial blood gases: pH, 7.30; $Paco_2$, 60 mm Hg; Pao_2, 49 mm Hg on Fio_2 50%, inspiratory pressure, 19/6 cm H_2O; and ventilation rate, 40 per minute.

A. Medical Disease and Differential Diagnosis

1. How would you classify prematurity? What are the common problems associated with prematurity?
2. What are the survival rates of preterm infants?
3. What are the incidence and survival rates of respiratory distress syndrome (RDS)? Discuss its pathophysiology.
4. What is bronchopulmonary dysplasia (BPD)? How would you treat it?
5. What are apnea spells? What are the possible causes of apneic spells?

6. Discuss the incidence and pathophysiology of PDA in preterm infants.
7. How would you make a diagnosis of PDA? Describe its treatment.
8. Would you give digitalis to treat congestive heart failure in preterm infants? Why?
9. How does indomethacin close the ductus? What are the adverse effects of indomethacin?
10. What is retinopathy of prematurity (ROP) (retrolental fibroplasia [RLF])? Discuss its etiology, pathophysiology, prognosis, and prevention.
11. Define neutral and critical temperatures. What are these values in the preterm neonate, in the term neonate, and in the adult? Discuss temperature regulation in the neonate.

B. Preoperative Evaluation and Preparation

1. How would you evaluate this patient preoperatively?
2. What are the normal values of arterial blood gases and pH in preterm and term pediatric patients?
3. Interpret the arterial blood gases: pH, 7.30; $Paco_2$, 60 mm Hg; Pao_2, 49 mm Hg; HCO_3^-, 20 mEq per L on 50% oxygen; and 6 cm H_2O of positive end-expiratory pressure (PEEP). How would you improve them?
4. What are the normal values of arterial blood pressure, heart rate, and respiratory rate for preterm infants?
5. What are the normal values of WBC, red blood cells (RBC), hemoglobin, glucose, electrolytes, calcium, blood urea nitrogen, and creatinine for preterm infants?
6. Would you transfuse blood to this patient preoperatively?
7. How would you interpret the urinalysis: specific gravity, 1.005; sugar, 1 +; protein, 1 +?
8. Would you correct a serum calcium level of 6.0 mg per dL? What other information would you like to have? Which contains more calcium, 10 mL of 10% calcium chloride or 10 mL of 10% calcium gluconate? Could you hyperventilate this child safely?
9. How would you premedicate this patient?

C. Intraoperative Management

1. What monitors would you use for this child during surgery?
2. How does the oxygen analyzer work?
3. What is the Doppler effect? How does the Doppler transducer measure blood pressure?
4. What is the mechanism of pulse oximetry? Why is it important to monitor arterial oxygen saturation? What levels of arterial oxygen saturation would you like to keep during surgery?
5. How would you maintain the patient's body temperature?
6. How do the anesthetic requirements of the preterm infant differ from those of the adult?
7. What size endotracheal tube would you have used if the patient had not been intubated?
8. How would you have induced anesthesia if the patient had not been intubated?
9. How would you maintain anesthesia?
10. How would you ventilate the patient? What tidal volume, respiratory rates, and FIO_2 would you set for the infant?
11. Discuss blood and fluid therapy in this preterm infant.

12. During dissection of the ductus arteriosus, the arterial oxygen saturation dropped from 92% to 80% and the heart rate decreased from 140 beats per minute to 80 beats per minute. What were the causes? How would you correct this situation?

D. Postoperative Management

1. Would you reverse the muscle relaxants and extubate the patient at the end of surgery?
2. How can one minimize the risk of transporting the patient to the neonatal intensive care unit (ICU) after surgery?
3. The patient's condition deteriorated postoperatively in the ICU. Physical examination revealed persistent cardiac murmur. What was the possible diagnosis?

A. Medical Disease and Differential Diagnosis

A.1. How would you classify prematurity? What are the common problems associated with prematurity?

Live born infants delivered before 37 weeks from the first day of the last mentstrual period are termed premature by the World Health Organization. Preterm infants can be classified into three groups, as shown in Table 44.1. Infants of borderline prematurity usually require no special care, but, because of their susceptibility to RDS, they should be observed closely for 24 to 48 hours in the newborn nursery. Further, those with a poor suck reflex may require gavage feedings. Infants classified as moderately premature require intense neonatal care, and neonatal mortality correlates inversely with gestational age. Neonates of extreme prematurity constitute only

Table 44.1 Classification of Prematurity

	BORDERLINE PREMATURITY	MODERATE PREMATURITY	EXTREME PREMATURITY
Gestational age (wk)	36–37	31–35	24–30
Percentage live births	16%	6%–7%	<1%
Weight (g)	2,500–3,200	1,500–2,500	500–1,500
Associated problems	Poor suck	Poor suck	Poor suck
	RDS	RDS	RDS
	Temperature regulation	Temperature regulation	Temperature regulation
		Sepsis	Sepsis
		Intracranial hemorrhage	Intracranial hemorrhage
			Necrotizing enterocolitis
			Congestive heart failure
			Birth asphyxia
Level of care	Careful observation in newborn nursery	Neonatal ICU	Neonatal ICU

ICU, intensive care unit; RDS, respiratory distress syndrome.

1% of all preterm infants; however, mortality in this group is extremely high, accounting for greater than 70% of all neonatal deaths. Furthermore, morbidity in surviving infants is substantial, often secondary to irreversible neurologic or respiratory insult.

Behrman RE, Kliegman RM, Jenson HB, et al., eds. *Nelson Textbook of Pediatrics*. 18th ed. Philadelphia: WB Saunders; 2007:701–710.

Cote C, Lerman J, Todres I. *Practice of Anesthesia in Infants and Children*. 4th ed. Saunders/Elsevier; 2009:735.

Gregory GA, ed. *Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 2002:369.

A.2. What are the survival rates of preterm infants?

The survival rates of preterm infants depend mainly on their maturity or birth weights. Because of the advancement in neonatal care, survival rates have increased twofold in the last two decades. Recently, the survival rates for infants with birth weights 500 to 750 g, 750 to 1,000 g, 1,000 to 1,250 g, 1,250 to 1,500 g, and 1,500 to 2,000 g have been approximately 53.9%, 86.3%, 94%, 96.8%, and 97%, respectively. Recent reports showed the survival rates for premature infants born at 24, 25, and 26 weeks' gestation to be 43%, 74%, and 83%, respectively.

Behrman RE, Kliegman RM, Jenson HB, et al., eds. *Nelson Textbook of Pediatrics*. 18th ed. Philadelphia: WB Saunders; 2007:701–710.

Cote C, Lerman J, Todres I. *Practice of Anesthesia in Infants and Children*. 4th ed. Saunders/Elsevier; 2009:735.

Gregory GA, ed. *Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 2002:370.

NICHD Neonatal Research Network. *Very low birth weight outcomes of the National Institute of Child Health and Human Development Neonatal Research Network*, Jan 1995 through Dec. 1996.

A.3. What are the incidence and survival rates of respiratory distress syndrome (RDS)? Discuss its pathophysiology.

RDS, formerly called hyaline membrane disease, is common in preterm infants. RDS is a life-threatening condition associated with 50% to 75% of all deaths of premature infants. It occurs three times more often in those born by cesarean section than in those born vaginally. The incidence of RDS depends on the birth weight. It happens in 86% of preterm infants weighing 501 to 750 g; 79% of preterm infants weighing 751 to 1,000 g; 48% of preterm infants weighing 1,001 to 1,250; and 27% of preterm infants weighing 1,251 to 1,500 g.

The survival rate has increased dramatically over the last 50 years. Survival depends on the infant's size. Ninety percent of those weighing 900 to 1,000 g survive, whereas approximately 70% of those weighing 500 to 700 g survive. Recently, an increase in survival and a decrease in severity of RDS have been associated with maternal steroid administration and routine administration of exogenous surfactant into the lungs of neonates of less than 28 weeks' gestation at birth. This may pose a problem for the anesthesiologist if these patients require surgery. Ventilation with high positive pressures and large volumes increases the likelihood of pulmonary gas leaks, pneumothorax, and lung injury.

Physical examination of the infant with RDS will likely reveal cyanosis, tachypnea, intercostal retractions, and bilateral rales that fail to clear with suctioning. An arterial blood gas sample will demonstrate hypoxemia, metabolic acidosis, and respiratory alkalosis; a chest radiograph will show diffuse, hazy ("ground glass") infiltrates.

Deficiency of the alveolar phospholipid surfactant is thought to be the cause of RDS. The surfactant is produced by the type II alveolar cells and is necessary for the maintenance of alveolar stability. Surfactant production is usually inadequate before 35 weeks of gestational age. In its absence, alveolar collapse and a decrease in functional residual capacity (FRC) occur, with consequent right-to-left shunting, arterial hypoxemia, and metabolic acidosis. Administration of betamethasone to women 48 hours before the delivery of fetuses less than 34-week gestation significantly reduces the incidence, mortality, and morbidity of RDS.

Andropolous D, Russell IA, Stayer S, eds. *Anesthesia for Congenital Heart Disease*. 2nd ed. Wiley-Blackwell; 2010:374.

Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's Anesthesia for Infants and Children*. 8th ed. Philadelphia: Mosby, Elsevier Science; 2010:696–697.

Gregory GA, ed. *Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 2002:370.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Coexisting Disease*. 5th ed. New York: Churchill Livingstone; 2008:585–586.

A.4. What is bronchopulmonary dysplasia (BPD)? How would you treat it?

BPD is defined as oxygen dependence at 36 weeks postconceptual age with oxygen requirements to maintain Pao2 > 50 mm Hg beyond 28 days of life in infants with birth weight less than 1,500 g. BPD is a chronic lung disease as a result of mechanical ventilation, oxygen toxicity, infection, or a combination of these factors. It includes interstitial fibrosis, lobar emphysema, and components of reactive airway disease, and may render the baby oxygen, steroid, or ventilator dependent. With progressive disease, it may lead to pulmonary hypertension and right heart failure. It usually progresses through four stages:

Stage I: At 2 to 3 days of age, the chest radiograph shows classic RDS. There are atelectasis, hyaline membrane, hyperemia, lymphatic dilation, metaplasia, and necrosis of bronchiolar mucosa.

Stage II: At 4 to 10 days of age, the chest radiograph shows obscure cardiac borders and nearly complete opacification of lung fields. The pathology reveals necrosis and repair of epithelium, persisting hyaline membrane, emphysematous coalescence of alveoli, and thickening of alveolar and capillary membranes.

Stage III: At 10 to 20 days of age, the chest radiograph shows small rounded areas of sponge-like radiolucency. There are few hyaline membranes, regeneration of clear cells, bronchiolar metaplasia, mucous secretion, emphysematous alveoli, and focal thickening of basement membrane.

Stage IV: After 30 days of age, the radiolucent areas seen in stage III enlarge and alternate with thin strands of radiodensity. The pathology reveals emphysematous alveoli and marked hypertrophy of epithelium.

BPD causes maldistribution of ventilation and perfusion, resulting in hypoxemia and hypercarbia. The treatment is supportive. The goals of treatment are to minimize the F_{IO_2} and mean airway pressure, reduce the amount of lung water with diuretics (furosemide 5 to 10 mg per kg every 6 hours), and to support cardiac contractility with inotropes.

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Behrman RE, Kliegman RM, Jenson HB, et al., eds. *Nelson Textbook of Pediatrics*. 18th ed. Philadelphia: WB Saunders; 2007:731–740.

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Davis PJ, Cladis FP, Motoyama EK, eds. *Smith's anesthesia for infants and children*. 8th ed. Philadelphia: Mosby, Elsevier Science; 2010.

Gregory GA, ed. *Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 2002:370.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Coexisting Disease*. 5th ed. New York: Churchill Livingstone; 2008:586–587.

A.5. What are apnea spells? What are the possible causes of apneic spells?

Apnea spells are defined as cessation of breathing lasting more than 20 seconds or more than 10 seconds and produces oxygen desaturatuion and bradycardia. Apneic spells are common in preterm infants, especially after the first week of life and almost universal in infants who are less than 1,000 g at birth. The causes are multiple and include the following:

- Hypothermia or hyperthermia
- Hypoglycemia or hyperglycemia
- Hypocalcemia or hypercalcemia
- Hypovolemia or hypervolemia
- Anemia
- Decreased FRC
- PDA
- Constipation
- Hypothyroidism
- Immature brain stem function
- Lack of type I muscle fibers in diaphragm
- Excessive handling
- Sepsis
- Gastroesophageal reflux disease

Repeated apnea increases the likelihood of central nervous system damage because of repeated episodes of hypoxemia. Infants who have apneic spells do not breathe during anesthesia; therefore, they should be ventilated throughout anesthesia, including the induction phase. Inhaled and intravenous anesthetics affect the control of breathing and contribute to upper airway obstruction, thereby increasing the likelihood of apnea during the postoperative period, especially in preterm infants less than 60 weeks postconception age.

Behrman RE, Kliegman RM, Jenson HB, et al., eds. *Nelson Textbook of Pediatrics*. 18th ed. Philadelphia: WB Saunders; 2007:729.

Cote C, Lerman J, Todres I. *Practice of Anesthesia in Infants and Children*. 4th ed. Saunders/Elsevier; 2009:736.

Gregory GA, ed. *Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 2002:370–371.

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A.6. Discuss the incidence and pathophysiology of PDA in preterm infants.

Fifty percent of infants weighing less than 1,000 g and 20.2% of infants under 1,750 g have hemodynamically significant PDA. In term infants, the ductus arteriosus closes soon after birth in response to the increased arterial oxygen tension. However, in preterm infants, it has a thinner, poorly contractile muscular layer with diminished responsiveness to the increasing oxygen levels after birth. In addition, preterm infants often suffer from hypoxemia because of RDS, so that there are both a reduced

stimulus to and a reduced response to physiologic closure. As many as 20% of neonates with RDS have a PDA. However, on the third to fifth day of life, some resolution of the RDS usually occurs, with a concurrent decrease in pulmonary resistance. This allows blood shunting from the systemic to the pulmonary circulation by way of the PDA, resulting in pulmonary vascular overload and ultimately left heart failure. The pulmonary congestion worsens respiratory failure, resulting in further hypoxemia and CO_2 retention.

Cote C, Lerman J, Todres I. *Practice of Anesthesia in Infants and Children*. 4th ed. Saunders/Elsevier; 2009:743.

Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2005:412–416.

Sethuraman G, Doty CI. Patent ductus arteriosus. eMedicine from WebMD, 2006.

A.7. How would you make a diagnosis of PDA? Describe its treatment.

The diagnosis of PDA in preterm infants may be suspected when there is sudden increase in respiratory failure, tachycardia, tachypnea, and a widened pulse pressure. The typical continuous or machinery murmur of PDA is usually not present in this population, but a systolic murmur, sometimes extending into diastole, and a hyperdynamic precordium are nearly always present. The diagnosis is confirmed by echocardiography that demonstrates left atrial enlargement. Two-dimensional echocardiography can identify the aortic end of the ductus. Continuous-wave Doppler can detect abnormal flow in the pulmonary artery. Color Doppler can visualize the jet of abnormal flow.

The initial treatment of PDA is medical. It includes fluid restriction and administration of diuretics and indomethacin. Indomethacin, 0.1 to 0.2 mg per kg, three doses for every 12 hours, usually closes the ductus within 24 hours. If the ductus fails to close with medical treatment, surgical ligation is indicated. There is now the option of percutaneous closure of PDA with an Amplatzer Duct Occluder.

Andropolous D, Russell IA, Stayer S, eds. *Anesthesia for Congenital Heart Disease*. 2nd ed. Wiley-Blackwell; 2010:374.

Cote C, Lerman J, Todres I. *Practice of Anesthesia in Infants and Children*. 4th ed. Saunders/Elsevier; 2009:743.

Gregory GA, ed. *Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 2002:349–350.

Pass RH, Hijazi Z, Hsu DT, et al. Multicenter USA amplatzer patent ductus arteriosus occlusion device trial: initial and one year results. *J Am Coll Cardiol*. 2004;44:513–519.

A.8. Would you give digitalis to treat congestive heart failure in preterm infants? Why?

Digitalis should not be given to small preterm infants because it does not effectively improve stroke volume or ventricular emptying. However, it does decrease the heart rate, resulting in detrimental decrease in cardiac output. Meanwhile, digitalis toxicity increases mortality in preterm infants.

Berman W Jr, Dubynsky O, Whitman V, et al. Digoxin therapy in low birth weight infants with patent ductus arteriosus. *J Pediatr*. 1978;93:652.

Gregory GA, ed. *Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 2002:349.

A.9. How does indomethacin close the ductus? What are the adverse effects of indomethacin?

The ductus arteriosus functionally closes shortly after birth in term infants when the vascular smooth muscle contracts. The muscular contraction of the ductus is initiated by the increased oxygen content and is influenced by other factors, such as release of vasoactive substances, the relative resistances in the aorta and pulmonary artery, and the differences in sensitivity of the vessel to oxygen. The ductus arteriosus produces several prostaglandins, including PGI_2 and PGE_2; both prostaglandins relax the smooth muscle of the ductus and keep the ductus patent. Meanwhile, the ductus of preterm infants is far more sensitive to the vasodilating effects of prostaglandins than is the ductus of term infants. Indomethacin is one of the most potent inhibitors of the prostaglandin-forming cyclooxygenase. Therefore, indomethacin decreases the synthesis of prostaglandins, resulting in closure of the ductus. Adverse effects of indomethacin include decreased mesenteric, renal, and cerebral blood flow. Ibuprofen is another nonselective cyclooxygenase inhibitor that can be used effectively to treat PDA and has less side effects on organ blood than indomethacin, although there is no clinical data to support its use in place of indomethacin.

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Clyman RI. Ontogeny of the ductus arteriosus response to prostaglandins and inhibitors of their synthesis. *Semin Perinatol*. 1980;4:115.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Coexisting Disease*. 5th ed. New York: Churchill Livingstone; 2008:47.

Wyllie J. Treatment of patent ductus arteriosus. *Semin Neonatol*. 2003;8:425–432.

A.10. What is retinopathy of prematurity (ROP) (retrolental fibroplasia [RLF])? Discuss its etiology, pathophysiology, prognosis, and prevention.

Some degree of ROP occurs in approximately 50% of infants weighing 1,000 to 1,500 g at birth, 78% of those weighing 750 to 999 g, and more than 90% of those weighing less than 750 g. At stage 3, ROP was not noted in infants with birth weight more than 1,500 g. No ROP was noted in infants born more than 32 weeks' gestational age. ROP begins with retinal vascular obliteration, which is followed by increased vascularity, hemorrhage, cicatrization, and finally retinal detachment. ROP refers to all stages of the disease and its sequelae. RLF, the term previously used for this disease, described only the cicatricial stages.

The factors that cause ROP and determine its outcome are not fully known, but prematurity, the degree of retinal immaturity at birth, and days on supplemental oxygen therapy are major factors. Other contributing factors include respiratory distress, apnea, bradycardia, heart disease, infection, hypoxia, hypercarbia, acidosis, anemia, and the need for transfusion. The presence of fetal hemoglobin may protect against ROP, and patients transfused with adult blood may be at great risk for developing ROP. Generally, the lower the birth weight and the sicker the infant, the greater the risk for ROP.

The retinal vasculature in the developing fetus spreads outward from the optic disc, reaching the nasal side of the retinal periphery by 36 weeks' gestational age and the temporal side at 40 weeks. Classically, it was postulated that hyperoxia constricts the retinal arterioles, resulting in swelling and degeneration of the endothelium. This causes paradoxical retinal ischemia in spite of systemic hyperoxia. When normoxic conditions are restored, vascularization resumes in an aberrant manner, leading to retinal detachment and blindness. ROP is divided into five stages:

Stage 1: A thin white line separates the posterior vascularized portion of the retina from the anterior avascular retina.

Stage 2: The demarcation line increases in volume and elevates. At this point, it is known as the "ridge". The changes in stage 1 and 2 regress in 80% of patients. Between 5% and 10% of premature infants with stage 1 and 2 disease progress to stage 3.

Stage 3: Tissue proliferation develops from the ridge, usually posteriorly. Stage 3 can be mild, moderate, or severe, depending on the volume of the extraretinal tissue.

Stage 4: Partial retinal detachment occurs with the macula still attached (stage 4a). The macula is detached in stage 4b.

Stage 5: Total retinal detachment occurs.

Eighty-five percent of ROP cases undergo spontaneous recovery. Mild ROP regresses in 2 to 3 months, and moderate ROP in 6 months. The most severe ROP usually results in blindness or limited vision.

It is unclear what level of Pao_2 causes ROP, but a Pao_2 of 150 mm Hg for as short a time as 1 to 2 hours can do so. Furthermore, the retinal vessels of these neonates certainly constrict maximally with a Pao_2 of 100 mm Hg. In addition, it is also possible that ROP might develop at lower Pao_2 levels because infants of this age are normally exposed to a much lower Pao_2 (30 to 40 mm Hg) in utero than the levels found during the neonatal period. Therefore, in order to reduce the possibility of ROP, it is wise to maintain the Pao_2 levels between 50 and 70 mm Hg or the saturation of oxygen (Sao_2) between 87% and 92% for infants <44 to 50 weeks' gestation. However, prevention of ROP ultimately depends on the prevention of premature birth and its attendant problems. Oxygen alone is neither sufficient nor necessary to produce ROP, and no safe level of oxygen has yet been determined. Each infant must be treated with whatsoever is necessary to sustain life and neurologic function. Some investigations have suggested the use of vitamin E for its antioxidant effects in infants at risk for ROP. However, its efficacy has not been proved.

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Cote C, Lerman J, Todres I. *Practice of Anesthesia in Infants and Children*. 4th ed. Saunders/Elsevier; 2009:687–738.

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Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Coexisting Disease*. 5th ed. New York: Churchill Livingstone; 2008:588–589.

Hussain N, Clive J, Bhandari V. Current incidence of retinopathy of prematurity, 1989–1997. *Pediatrics*. 1999;104(3):e26.

Stark DJ, Manning LM, Lenton L. Retrolental fibroplasia today. *Med J Aust*. 1981;1:275.

A.11. Define neutral and critical temperatures. What are these values in the preterm neonate, in the term neonate, and in the adult? Discuss temperature regulation in the neonate.

Neutral temperature is the ambient temperature that results in minimal oxygen consumption. Critical temperature is the ambient temperature below which an unclothed, unanesthetized individual cannot maintain a normal core temperature (see Table 44.2).

Normally, body heat is lost by conduction, convection, radiation, and evaporation. The neonate is particularly susceptible to heat loss owing to a large surface: volume ratio, lack of insulating fat, and naturally flaccid and open posture. When stressed by a cold environment, vasoconstriction occurs, but the neonate is unable to shiver. Further

Table 44.2 Neutral and Critical Temperature

	NEUTRAL TEMPERATURE (°C)	CRITICAL TEMPERATURE (°C)
Preterm neonate	34	28
Term neonate	32	23
Adults	28	1

cold stress stimulates norepinephrine release, promoting the exothermic metabolism of brown fat deposits in an attempt to maintain core temperature. Continued cold stress often results in episodes of bradycardia, apnea, hypoglycemia, and metabolic acidosis.

When the infant's rectal temperature reaches 36.6° C to 37.3° C (97.88° F to 99.14° F), dilation of peripheral vessels occurs. The term neonate will perspire at 37.2° C (98.96° F) in an attempt to maintain a normal core temperature, whereas those infants born before 37 weeks' gestation are unable to sweat.

Cote C, Lerman J, Todres I. *Practice of Anesthesia in Infants and Children*. 4th ed. Saunders/Elsevier; 2009:738.

Gregory GA, ed. *Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 2002:347.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Coexisting Disease*. 5th ed. New York: Churchill Livingstone; 2008:584–585.

B. Preoperative Evaluation and Preparation

B.1. How would you evaluate this patient preoperatively?

The preoperative evaluation of preterm infants should be based on a clear understanding of the pathophysiology of prematurity. The preoperative evaluation of this patient should begin with a careful review of the medical record, followed by a systematic physical examination and laboratory evaluation, specifically:

- *History*. Birth trauma, asphyxia, maternal drug history, respiratory, cardiovascular, and fluid status
- *Physical examination*. Evaluation of the airway, cardiopulmonary system, fluid status (skin texture, turgor, mucous membranes, and fontanelles), and abdominal examination
- *Laboratory data*. WBC count; hemoglobin and hematocrit; serum electrolytes; serum coagulation profile, including prothrombin time, partial thromboplastin time, and platelet count; serum calcium and serum protein; arterial blood gases; urinalysis and urine-specific gravity; chest and abdominal radiographs

B.2. What are the normal values of arterial blood gases and pH in preterm and term pediatric patients?

The normal blood gas and pH values for pediatric patients are shown in Table 44.3. The normal pH and $Paco_2$ values for pediatric patients are similar to those for adults, whereas the normal Pao_2 values are lower in pediatric patients than in adult patients.

Gregory GA, ed. *Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 2002:257, 355.

Table 44.3 Normal Values of Arterial Blood Gases and pH in Pediatric Patients

AGE	PRETERM	TERM	1 MONTH	1 YEAR
pH	7.37 ± 0.03	7.40 ± 0.02	7.41 ± 0.04	7.39 ± 0.02
Pao_2 (mm Hg)	60 ± 8	70 ± 11	95 ± 8	93 ± 10
$Paco_2$ (mm Hg)	37 ± 6	39 ± 7	40 ± 6	41 ± 7

B.3. Interpret the arterial blood gases: pH, 7.30; $Paco_2$, 60 mm Hg; Pao_2, 49 mm Hg; HCO_3^-, 20 mEq per L on 50% oxygen; and 6 cm H_2O of positive end-expiratory pressure (PEEP). How would you improve them?

The blood gases show respiratory and metabolic acidosis. The Pao_2 of 49 mm Hg is low, but acceptable for preterm infants with chronic lung disease. In order to prevent ROP, it is wise to keep Pao_2 between 50 and 70 mm Hg. $Paco_2$ of 60 mm Hg indicates hypoventilation, which can be corrected by increasing respiratory rate or tidal volume. In order to avoid the pulmonary oxygen toxicity, FIo_2 should be lowered to less than 40% by increasing levels of PEEP. Mild metabolic acidosis may be corrected by hyperventilation and by improving fluid balance and circulation.

B.4. What are the normal values of arterial blood pressure, heart rate, and respiratory rate for preterm infants?

The blood pressure is related to the size of infants, as shown in Table 44.4. The heavier the birth weight, the higher the blood pressure is. The normal heart rate is 120 to 160 beats per minute. The respiratory rate is normally between 30 and 60 breaths per minute. However, it can increase to 100 to 150 breaths per minute depending on how severely the lung compliance is decreased.

Cote C, Lerman J, Todres I. *Practice of Anesthesia in Infants and Children*. 4th ed. Saunders/Elsevier; 2009:18.

Gregory GA, ed. *Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 2002:251.

B.5. What are the normal values of WBC, red blood cells (RBC), hemoglobin, glucose, electrolytes, calcium, blood urea nitrogen, and creatinine for preterm infants?

The WBC count usually ranges from 9,000 to 30,000 per mm^3 at birth and decreases to 5,000 to 20,000 per mm^3 during the fifth week of life.

Table 44.4 Normal Blood Pressure of Infants Weighing between 1,000 and 4,000 g

	BIRTH WEIGHT (g)			
	1,000	2,000	3,000	4,000
Systolic BP (mm Hg)	50 ± 10	55 ± 10	60 ± 10	70 ± 10
Diastolic BP (mm Hg)	25 ± 10	30 ± 10	35 ± 10	40 ± 10
Mean BP (mm Hg)	35 ± 10	40 ± 10	45 ± 10	50 ± 10

BP, blood pressure.

The normal RBC and hemoglobin are 5.1 ± 1.0 × 10^6 per mm^3 and 19.5 ± 5.0 g per dL, respectively, at birth and decrease to 4.5 ± 0.7 × 10^6 per mm^3 and 12.2 ± 2.3 g per dL, respectively, at 3 months of age. At birth, most of the hemoglobin is fetal hemoglobin, which has a greater affinity for oxygen. Therefore, the oxygen saturation (and content) of blood for a given Pao_2 is higher. By 7 months of age, the circulating hemoglobin is of the adult type.

The normal blood glucose level is between 45 and 90 mg per dL. A glucose level below 40 mg per dL is common in preterm infants. It should be corrected with a bolus of 10% to 20% glucose (2 to 5 g/kg) given over 5 minutes, followed by a continuous infusion of glucose. Severe hypoglycemia (<10 mg/dL) may cause brain damage.

The serum calcium concentration of preterm infants is normally lower than that of term infants because preterm infants have decreased serum proteins. Normal calcium level is over 8.0 mg per dL.

The normal values of sodium, potassium, and chloride are 135 to 145, 3.0 to 5.0, and 105 to 115 mEq per L, respectively.

The creatinine levels of term infants at birth are 0.6 to 1.2 mg per dL, but, within 1 month, fall to levels of 0.1 to 0.2 mg per dL. Preterm infants have relatively high serum creatinine levels compared with term infants. They are 0.8 to 1.8 mg per dL at birth and fall to 0.2 to 0.8 mg per dL in 1 month.

The normal blood urea nitrogen level is 10 to 20 mg per dL in term infants, whereas it is 16 to 28 mg per dL in preterm infants.

Behrman RE, Kliegman RM, Jenson HB, Stanton BF, eds. *Nelson Textbook of Pediatrics*. 18th ed. Philadelphia: WB Saunders; 2007:2944–2949.

Gregory GA, ed. *Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 2002:350–357.

B.6. Would you transfuse blood to this patient preoperatively?

The patient had a hemoglobin of 11 g per dL; we would not transfuse blood to this patient. To ensure oxygen-carrying capacity, most clinicians agree that a hemoglobin of 10 g per dL is the lowest acceptable level if cardiorespiratory disease exists. If infants are well, a hemoglobin level of above 7.0 g per dL is usually tolerable.

Cote C, Lerman J, Todres I. *Practice of Anesthesia in Infants and Children*. 4th ed. Saunders/Elsevier; 2009:739.

Gregory GA, ed. *Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 2002:357.

B.7. How would you interpret the urinalysis: specific gravity, 1.005; sugar, 1 +; protein, 1 +?

In infants weighing 1,000 to 3,300 g, the normal urine-specific gravity is 1.005 to 1.010. A urine specific gravity of greater than 1.020 suggests dehydration.

Glucosuria 1 + normally presents in 13% of preterm infants who are less than 34 weeks' gestational age because the preterm infant has a decreased renal tubular reabsorption for glucose. After 34 weeks of gestational age, glucosuria is usually associated with serum hyperglycemia.

Albumin is normally filtered by the glomerulus and is completely reabsorbed. However, because of tubular immaturity, 16% to 21% of preterm infants have proteinuria.

Cote C, Lerman J, Todres I. *Practice of Anesthesia in Infants and Children*. 4th ed. Saunders/Elsevier; 2009:170.

Grant BS Jr. Developmental patterns of renal functional maturation compared in the human neonate. *J Pediatr*. 1978;92:705.

Jones MD, Gersham EL, Battaglia FC. Urinary flow rates and urea excretion rates in newborn infants. *Biol Neonate*. 1972;21:321.

Rhodes PG, Hammel CL, Berman LB. Urinary constituents of the newborn infant. *J Pediatr*. 1962;60:18.

B.8. Would you correct a serum calcium level of 6.0 mg per dL? What other information would you like to have? Which contains more calcium, 10 mL of 10% calcium chloride or 10 mL of 10% calcium gluconate? Could you hyperventilate this child safely?

Normally, the serum calcium is maintained at 8.0 mg per dL; however, in the preterm infant, a level of 7.0 mg per dL is acceptable. This child's serum calcium is 6.0 mg per dL. Therefore, supplementation with 30 to 100 mg per kg of calcium gluconate or 10 to 20 mg per kg of calcium chloride is appropriate.

Hypocalcemia in neonate is defined as serum calcium less than 3.5 mEq per L or serum ionized calcium less than 1.5 mEq per L. When evaluating the serum calcium levels, it is important to know the serum protein concentration; neonatal hypocalcemia is usually due to hypoproteinemia. It is also important to determine the ionized calcium concentration (usually 45% of the total calcium concentration), because this is the calcium immediately available at the cellular level. The chloride molecule is approximately one-third the weight of the gluconate molecule. For this reason, approximately three times more calcium is given when an equivalent volume of calcium chloride is administered instead of 10% calcium gluconate. Respiratory alkalosis following hyperventilation will reduce serum ionized calcium levels and, for this reason, should be avoided in this infant.

Gregory GA, ed. *Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 2002: 159,351–357.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Coexisting Disease*. 5th ed. New York: Churchill Livingstone; 2008:591–592.

B.9. How would you premedicate this patient?

Children under 1 year of age do not usually need sedation. However, atropine, 0.01 to 0.02 mg per kg, may be given to attenuate the vagal response to a host of different stimuli.

Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2005:412–416.

C. Intraoperative Management

C.1. What monitors would you use for this child during surgery?

Proper monitoring of this child for safe administration of anesthesia includes the following:

- *Respiratory*. Precordial or esophageal stethoscope, end-tidal CO_2, inspiratory oxygen monitor, pulse oximeter, arterial blood gases, inspiratory pressure gauge
- *Cardiovascular*. Precordial or esophageal stethoscope, electrocardiogram, blood pressure cuff and Doppler transducer, and urinary bag

- *Thermoregulatory*. Esophageal or axillary temperature probe with servoloop overhead heater, and thermal blanket

If the patient has an umbilical artery catheter in place, it is useful for the measurement of blood pressure and arterial blood gases. However, it is probably unnecessary to establish an arterial line for the surgery alone because invasive monitoring in this age group is not without risk.

C.2. How does the oxygen analyzer work?

Oxygen analysis can be done by either parametric or ampometric analysis. Parametric analysis is based on the fact that oxygen is a dipole molecule. When a gas containing oxygen is passed through a magnetic field, the gas is deflected in proportion to the concentration of oxygen. Sensors can detect this deflection and give a readout of oxygen concentration. Ampometric analysis can be done with one of the two devices: the galvanic cell analyzer and the polarographic cell analyzer. In the galvanic or fuel cell analyzer, oxygen diffuses through a membrane of the sensor into an electrolyte solution from which the oxygen absorbs electrons and forms hydroxide ions. The hydroxide ions then diffuse to a lead anode where oxidation to lead oxide and water occurs with the resultant liberation of free electrons. An electron flow (current) is thereby generated between the anode and the cathode, which is proportional to the oxygen level at the sensor. This current is directly displayed by a meter that indicates oxygen percentage. These devices are relatively inexpensive to purchase but carry a high operating cost because the sensor is eventually exhausted and must be replaced.

The polarographic cell, or Clark electrode, uses a battery to induce a negative potential of 0.75 V between the anode and the cathode. As oxygen diffuses across a membrane and into the electrolyte solution separating the anode and cathode, the polarizing voltage at the cathode causes electrons to combine with oxygen molecules, reducing them to hydroxide ions. The hydroxide ions then move to the anode, causing electron flow (current) that is proportional to the initial oxygen concentration. This flow is read by a meter that translates to oxygen percentages. These monitors are initially more expensive than galvanic cell monitors, but they are less expensive to maintain, requiring only inexpensive electrolyte solution and battery replacement.

Miller RD, Eriksson L, Fleisher L, eds. *Miller's Anesthesia*. 7th ed. Churchill Livingstone/Elsevier; 2010:670.

Saidman LJ, Smith NT, eds. *Monitoring in Anesthesia*. 3rd ed. Boston: Butterworth-Heinemann; 1993:384.

C.3. What is the Doppler effect? How does the Doppler transducer measure blood pressure?

In 1841, Christian Doppler noted the change in observed frequency from a constant frequency sound generator when the source moved with respect to the observer. Ballot confirmed this "Doppler effect" in 1845 with the simple example of the frequency increase in a train's steam whistle as the train approached an observer. In the 1960s, Ware described a practical ultrasonic system for transducing arterial wall motion to obtain blood pressure. The ultrasonic system consists of an occlusive cuff and a dual crystal ultrasonic transducer placed over the artery distal to the occlusion. One crystal transmits the ultrasonic signal, whereas the other receives the signal reflected from the artery. Although the cuff occludes the artery, there is no arterial wall movement and the crystal receives a signal with an unchanged frequency. When the cuff pressure falls below systolic pressure, arterial wall motion

occurs, causing a Doppler frequency shift, indicating systolic blood pressure. When the cuff pressure falls to diastolic pressure, the artery is open throughout the cycle: rhythmic arterial opening and closing does not occur and there is a loss of Doppler frequency shift. Therefore, one can easily and accurately obtain systolic and diastolic blood pressure.

Miller R, Eriksson L, Fleisher L, eds. *Miller's Anesthesia*. 7th ed. Churchill Livingstone/Elsevier; 2010:6.

Saidman LJ, Smith NT, eds. *Monitoring in Anesthesia*. 3rd ed. Boston: Butterworth-Heinemann; 1993:121.

C.4. What is the mechanism of pulse oximetry? Why is it important to monitor arterial oxygen saturation? What levels of arterial oxygen saturation would you like to keep during surgery?

The mechanism of pulse oximetry is described in Chapter 2, section C.10 and Chapter 58, section A.5.

Safe anesthesia practice requires the monitoring of arterial oxygen saturation in all patients to prevent hypoxia. However, in infants of less than 44 to 50 weeks, gestation, it is also vital to guard against hyperoxia, which may cause ROP.

The arterial oxygen saturation should be kept between 86% and 92% (some say 85% to 95%).

Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesi*a. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2005:412–416.

Purohit DM, Ellison RC, Fierler S, et al. Risks of retrolental fibroplasia: experience with 3025 premature infants. *Pediatrics*. 1985;76:339.

Wasunna A, Whitlaw AGL. Pulse oximetry in preterm infants. *Arch Dis Child*. 1987;62:957.

C.5. How would you maintain the patient's body temperature?

Hypothermia greatly increases the metabolic rate and oxygen consumption of preterm infants. The preterm infant is particularly susceptible to heat loss because of a large surface-to-volume ratio, lack of insulating fat, and a naturally flaccid and open posture. In addition, the preterm infant often has impaired thermal regulatory ability; therefore, all precautions must be taken to ensure normothermia. The patient may be transported to the operating room in a battery-operated transport incubator if available. Otherwise, the infant should be covered with Saran Wrap and a warm blanket, and a cap should be put on his or her head to prevent heat loss. The operating room should be warmed to 35° C to 37° C (95° F to 98.6° F) and a servo-controlled infrared heater placed over the operating table. A water-circulating heating blanket should be put under the table sheet and kept at 37° C to 38° C (98.6° F to 100.4° F). All extremities should be wrapped in sheet wadding. All intravenous fluids and inspired gases should be warmed and humidified to help maintain the patient's body temperature. If the facility is available, then in the very low birth weight infants, the procedure can be done at the bedside with the appropriate equipment and using the ICU ventilator for airway management. This helps minimize the risks associated with transportation and also minimize the incidence of hypothermia.

Gregory GA, ed. *Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 2002:358, 360.

C.6. How do the anesthetic requirements of the preterm infant differ from those of the adult?

Achieving proper anesthetic depth in the preterm infant presents a unique challenge to the anesthesiologist. Whereas anesthetic requirements (as determined by minimal alveolar concentration) are decreased in the preterm infant as compared with the adult, possibly due to immaturity of the central nervous system and to increase circulating concentrations of progesterone and β-endorphins. Cardiovascular sensitivity is greatly pronounced because of greater myocardial depression and a reduced peripheral response to catecholamines. Further, the baroreceptor reflex, often poorly developed in the preterm infant, is totally ablated by even light levels of inhalation anesthesia. Therefore, the preterm infant is extremely susceptible to anesthetic overdose, which produces cardiovascular depression leading to hypotension or cardiovascular collapse.

Unfortunately, an inadequate depth of anesthesia is also uniquely hazardous in the neonate. Because there is a lack of cerebral autoregulation, any systemic hypertension from inadequate depth of anesthesia may be transmitted directly to the cerebral circulation, resulting in intraventricular hemorrhage.

For these reasons, it is essential to carefully tailor anesthetic depth to surgical conditions, because the therapeutic margin between underdose and overdose is extremely narrow.

Gregory GA. The baroresponses of preterm infants during halothane anesthesia. *Can Anaesth Soc J*. 1982;29:105.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Coexisting Disease*. 5th ed. New York: Churchill Livingstone; 2008:584–585.

Lou HC, Lassen PH, Fris-Hansen B. Impaired autoregulation of cerebral blood flow in the distressed newborn infant. *J Pediatr*. 1979;94:118.

C.7. What size endotracheal tube would you have used if the patient had not been intubated?

The larynx of a full-term neonate usually accommodates a 3.0- or 3.5-mm endotracheal tube, whereas infants weighing less than 3,500 g tolerate a 3.0-mm tube. In infants weighing less than 1,500 g, a 2.5-mm (internal diameter) tube is usually recommended. The endotracheal tube should be large enough to allow easy ventilation but small enough to permit leaking of gas between the tube and trachea when the lung is ventilated with 15 to 20 cm H_2O pressure. However, a higher leak pressure of 25 to 35 cm H_2O may be aimed for when high peak inspiratory pressures may be required during anesthesia, for example, during a thoracotomy or an upper laparotomy, or if the patient has decreased pulmonary compliance.

Cote C, Lerman J, Todres I. *Practice of Anesthesia in Infants and Children*. 4th ed. Saunders/Elsevier; 2009:735.

Gregory GA, ed. *Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 2002:218.

C.8. How would you have induced anesthesia if the patient had not been intubated?

Preterm infants do need anesthesia for surgery. The patient should be preoxygenated with 100% oxygen, and ventilation should be controlled; otherwise, the preterm infant develops apnea and bradycardia. Anesthesia in the ICU is induced with fentanyl, 1 to

3 μg per kg. When the lid reflexes are lost, the infant is intubated after 0.05 to 0.1 mg per kg of pancuronium. After intubation, breath sounds should be checked bilaterally to ensure that the tube is properly positioned.

Alternatively, anesthesia may be induced in the operating room with an inhalation anesthetic such as sevoflurane followed by muscle relaxation with pancuronium or rocuronium before intubation.

Andropolous D, Russell IA, Stayer S, eds. *Anesthesia for Congenital Heart Disease*. 2nd ed. Wiley-Blackwell; 2010:376.

Robinson SR, Gregory GA. Fentanyl-air oxygen anesthesia for ligation of patent ductus arteriosus in preterm infants. *Anesth Analg*. 1981;60:504.

C.9. How would you maintain anesthesia?

Because preterm infants are extremely sensitive to cardiovascular depression from inhalation anesthetics, we prefer to use fentanyl with or without nitrous oxide for maintenance of anesthesia. Increments of fentanyl, 3 to 5 μg per kg, are titrated to maintain hemodynamic stability. A bolus injection of high-dose fentanyl, 30 to 50 μg per kg, often causes hypotension because the infant is usually dehydrated as a result of fluid restriction and diuretic therapy for congestive heart failure from PDA. Ketamine may be used alone or as a supplement to fentanyl-air-oxygen anesthesia.

Pancuronium, 0.1 mg per kg, is an attractive choice for muscle relaxation because it causes mild tachycardia and the infant's blood pressure is dependent on heart rate.

Cote C, Lerman J, Todres I. *Practice of Anesthesia in Infants and Children*. 4th ed. Saunders/Elsevier; 2009:743.

Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2005:412–416.

Robinson SR, Gregory GA. Fentanyl-air-oxygen anesthesia for ligation of patent ductus arteriosus in preterm infants. *Anesth Analg*. 1981;60:504.

C.10. How would you ventilate the patient? What tidal volume, respiratory rates, and FIO_2 would you set for the infant?

Controlled ventilation should be employed because preterm infants do not breathe well under anesthesia. The patient may be ventilated by hand with a Jackson-Reese device. The technique allows instantaneous compensation for changes in pulmonary compliance and resistance, especially during thoracotomy. It also permits the use of PEEP. If extra hands are not available, mechanical ventilation, preferably with a pediatric bellows, may be used to ventilate the infant.

During spontaneous respiration, normal tidal volume is 7 mL per kg for all ages. However, the ventilator tidal volumes calculated on the basis of body weight for adult patients, such as 10 mL per kg, are not applicable for pediatric patients, especially small infants. A large amount of ventilator-delivered tidal volume is lost through the large compression volume of the anesthesia breathing circuit and the leak around the uncuffed endotracheal tube. For example, if the compression volume of the anesthesia ventilator is 4.5 mL per cm H_2O (a value typical for adult ventilators) and the ventilator is set to deliver a 100 mL tidal volume to a patient at 20 cm H_2O peak inspiratory pressure, 90 mL is lost to compression volume: Only 10 mL is delivered to the patient. In addition, if pulmonary and chest wall compliances change during anesthesia and surgery, the delivered tidal volume to the patient will also be changed. Therefore, it is wise to set tidal volume whatever necessary to achieve the desired inspiratory

pressures, such as those used in the neonatal ICU before surgery. Usually the peak inspiratory pressures are set between 15 and 25 cm H_2O, depending on the patient's respiratory condition, to ensure adequate chest expansion.

The respiratory rates and inspiratory pressures are adjusted as needed to maintain the $Paco_2$ between 35 and 40 mm Hg or the end-tidal CO_2 between 30 and 35 mm Hg. The Fio_2 is adjusted to keep the Pao_2 between 50 and 70 mm Hg or the arterial oxygen saturation between 87% and 92% (practically 90% to 95%).

Gregory GA, ed. *Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 2002:359.

Robins L, Crooker D, Smith RM. Tidal volume losses of volume limited ventilators. *Anesth Analg*. 1967;46:428.

C.11. Discuss blood and fluid therapy in this preterm infant.

Fluid therapy should be aimed at correcting the preoperative deficit, providing maintenance fluid, and replacing intraoperative evaporative, third space, and blood loss.

Intraoperative blood loss must be carefully estimated by weighing the sponges and using small-calibrated suction bottles in plain view of the anesthesiologist. The preterm infant's blood volume is only 80 to 95 mL (85 to 100 mL per kg); therefore, even a 10 mL blood loss can be critical. Despite these precautions, estimation of blood loss is inevitably inaccurate because of the unmeasured loss in the drapes and tissues. For this reason, it is recommended that 125% to 150% of measured blood loss be replaced. Each milliliter of estimated blood loss is replaced with 3 mL of Ringer's lactate or 1 mL of 5% albumin in saline. If the hematocrit is low (<30%) to begin with, blood losses are replaced with packed RBC.

Maintenance fluids consisting of 5% dextrose in one-fourth strength normal saline are given at 4 mL per kg per hour, whereas evaporative and third-space losses are replaced with Ringer's lactate at 8 to 12 mL per kg per hour for abdominal or thoracic procedures. The adequacy of blood and fluid therapy may be ensured by stable blood pressure, normal central venous pressure (over 3 cm H_2O), and an adequate urine output of >0.75 mL per kg per hour and specific gravity of less than 1.010. In addition, the infant's fontanelle should be above the inner table of the skull if there is no volume depletion.

Cote C, Lerman J, Todres I. *Practice of Anesthesia in Infants and Children*. 4th ed. Saunders/Elsevier; 2009:737;743.

Gregory GA, ed. *Pediatric Anesthesia*. 4th ed. New York: Churchill Livingstone; 2002:360.

C.12. During dissection of the ductus arteriosus, the arterial oxygen saturation dropped from 92% to 80% and the heart rate decreased from 140 beats per minute to 80 beats per minute. What were the causes? How would you correct this situation?

Pediatric patients, especially preterm infants, develop hypoxemia quickly after hypoventilation because they have high metabolism (increased oxygen demand) and low FRC (decreased oxygen reserve). During dissection of the ductus arteriosus, the ipsilateral lung is retracted and compressed by the surgeon. Therefore, the pulmonary resistance increases and pulmonary compliance decreases. Consequently, the delivered tidal volume to the patient decreases and the gas leak around the endotracheal tube increases if the inspiratory pressures remain unchanged. Decreasing tidal volume causes hypoventilation, resulting in hypoxemia and CO_2 retention. In addition, compressing the lung tissue increases intrapulmonary shunt, which causes further hypoxemia. In pediatric

patients, bradycardia is most commonly caused by hypoxemia. During dissection of the ductus arteriosus, surgical manipulation of the vagus nerve and lung tissue may initiate vagal reflex, with resultant bradycardia.

The infant should be manually ventilated with 100% oxygen to correct hypoxemia and bradycardia. If bradycardia persists, atropine, 0.01 to 0.02 mg per kg, should be given. The surgical manipulation should be stopped and the collapsed lung reexpanded. Blood loss or hypovolemia should also be corrected.

When the hemodynamic status and oxygenation are stabilized, the F_{IO_2} and respiratory pressures should be adjusted to ensure adequate ventilation and oxygenation.

D. Postoperative Management

D.1. Would you reverse the muscle relaxants and extubate the patient at the end of surgery?

No. Postoperative ventilatory support would be necessary for this preterm infant with RDS; therefore, reversal of muscle relaxation and extubation are not indicated.

Cote C, Lerman J, Todres I. *Practice of Anesthesia in Infants and Children*. 4th ed. Saunders/Elsevier; 2009:744.

D.2. How can one minimize the risk of transporting the patient to the neonatal intensive care unit (ICU) after surgery?

The anesthesiologist's responsibilities do not end with the successful completion of the operative procedure. Removal of the surgical drapes must be done with caution to prevent inadvertent extubation or removal of the arterial or venous cannula. Transportation of the infant to the neonatal ICU is an extremely hazardous transition and requires watchful vigilance. Arrangements must be made in advance so that elevators are waiting and the nursery is ready to accept the patient. The anesthesiologist must accompany the child until satisfied that care has been appropriately transferred to the neonatal nursery staff.

The same monitors that were employed for surgery must be used in transport, including electrocardiogram and monitors for arterial blood pressure and oxygen saturation. Ventilation should be maintained by hand with a Jackson-Reese device or by a battery-operated transport ventilator, and the child should not be transported with 100% oxygen unless it was used for the operative procedure. A precordial stethoscope is especially helpful to monitor the adequacy of respiration and heart sounds. Finally, every effort to ensure thermal stability must be made, including the use of a heated Isolette (if possible), Saran Wrap, warm blankets, and a cap on the infant's head.

Miller RD, Eriksson L, Fleisher L, eds. *Miller's Anesthesia*. 7th ed. Churchill Livingstone/Elsevier; 2010:2637.

D.3. The patient's condition deteriorated postoperatively in the ICU. Physical examination revealed persistent cardiac murmur. What was the possible diagnosis?

It has been reported that a large ductus arteriosus arising from the aortic arch proximal to the subclavian artery creates the illusion of the arch, leading to surgical closure of the distal left pulmonary artery instead of ductus arteriosus (Fig. 44.1). A sign of

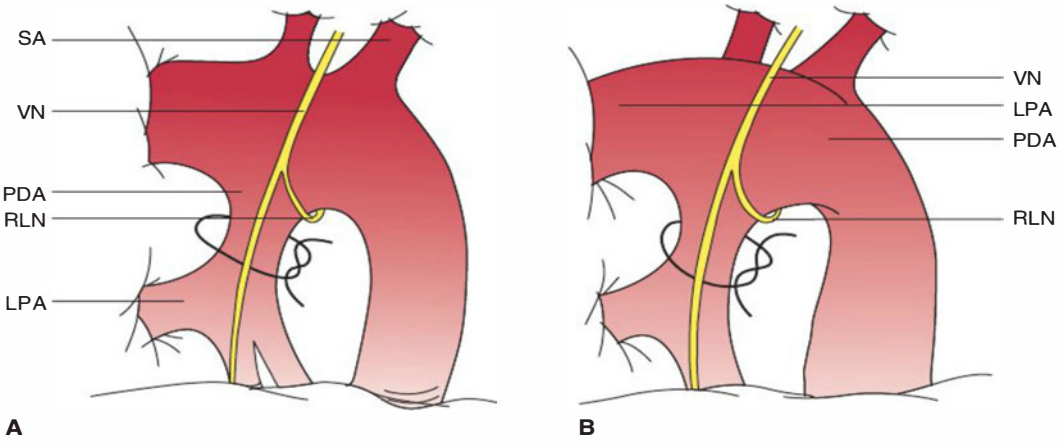


Figure 44.1 **A.** Anatomically atypical patent ductus arteriosus arising proximal to the left subclavian artery. **B.** Large patent ductus arteriosus sweeping into the descending aorta and appearing to be the arch. The ductus overlies the arch and hides it from view. A large distal left pulmonary artery is misinterpreted as the patent ductus (encircled by ligature). LPA, left pulmonary artery; PDA, patent ductus arteriosus; RLN, recurrent laryngeal nerve; SA, subclavian artery; VN, vagus nerve. (Adapted from Pontius RG, Danielson GK, Noonan JA, et al. Illusions leading to surgical closure to the distal left pulmonary artery instead of the ductus arteriosus. *J Thorac Cardiovasc Surg.* 1981;82:103–107.)

successful PDA ligation is an increase in diastolic blood pressure from the elimination of pulmonary runoff during diastole. To help identify the ductus, some surgeons place a temporary clip on the what they believe is the ductus and observe whether the diastolic pressure increases correspondingly.

In this case, the ductus arteriosus was not ligated; therefore, the ductus murmur persisted. Inadvertent ligation of the distal left pulmonary artery resulted in pulmonary ischemia distal to the ligation. Meanwhile, the right lung was further flooded with the shunted blood through the unligated PDA. The resultant ventilation/perfusion maldistribution ($\dot{V}/\dot{Q}$ abnormalities) caused further hypoxemia and CO_2 retention in this infant. The patient should be brought to the operating room for repair of the left pulmonary artery and ligation of the ductus arteriosus.

Miller RD, Eriksson L, Fleisher L, eds. *Miller's Anesthesia*. 7th ed. Churchill Livingstone/Elsevier; 2010:2637.

Pontius RG, Danielson GK, Noonan JA, et al. Illusions leading to surgical closure to the distal left pulmonary artery instead of the ductus arteriosus. *J Thorac Cardiovasc Surg*. 1981;82:103–107.

SECTION XI

Pain Management and Neuraxial Blocks

CHAPTER 45

Brachial Plexus Block

William Urmey

A 62-YEAR-OLD MAN

presents after sustaining a fall and proximal right humeral fracture. The patient's history is remarkable for hypertension and significant chronic obstructive pulmonary disease (COPD). He has a 30 pack-year cigarette smoking history. His only other remarkable history is that he claims to have fainted several times in his life. Recent pulmonary function tests 6 months before admission include a forced vital capacity (FVC) of 1.4 L (33% predicted). The patient's routine medications include atenolol and hydrochlorothiazide. Hydromorphone 1 mg was administered intravenously in the emergency room.

A. Medical Disease and Differential Diagnosis

1. What are the presenting problems in this patient?
2. What additional medical history would you want to obtain?
3. How can testing be done to evaluate severity of the patient's vasovagal syncope (neurocardiogenic bradycardia, asystole)?
4. What implications does the use of atenolol have on the patient's coexisting medical condition?
5. Why is immobilization of the arm important following humeral fracture?
6. What nerve is at particular risk for injury from humeral fracture?

B. Preoperative Evaluation and Preparation

1. What premedication would you order?
2. What are the respiratory effects of benzodiazepines?

C. Intraoperative Management

1. What anesthetic technique would you use?
2. Describe the relevant anatomy of the brachial plexus.
3. What relevant anatomic structures in the neck and below the neck can be injured or injected accidentally during brachial plexus block?
4. What regional technique would you choose to block the brachial plexus in this patient?
5. What are the advantages and disadvantages of the following blocks?
   a. Interscalene block
   b. Subclavian perivascular block
   c. Ultrasound-guided supraclavicular block
   d. Ultrasound-guided infraclavicular block
   e. Axillary block
6. Describe landmarks and procedures for interscalene block with nerve stimulation and ultrasound.
7. Describe landmarks and procedures for ultrasound-guided supraclavicular block.
8. Describe landmarks and procedure for ultrasound-guided infraclavicular block.
9. Describe landmarks and procedure for axillary brachial plexus block using a nerve stimulator.
10. The patient requests to have the interscalene block performed after you administer general anesthesia. Would you agree to this request?
11. What relevant respiratory complications or side effects are you concerned about in this patient?
12. What is the incidence of hemidiaphragmatic paresis following interscalene brachial plexus block? Can this complication be avoided by lowering the volume or concentration of local anesthetic injected? By using ultrasound-guided supraclavicular block?
13. Describe the pulmonary function changes that occur after interscalene brachial plexus block.
14. What would you do if the patient complained of dyspnea after you performed an interscalene block?
15. The surgeon prefers to perform the surgical procedure in the sitting position. What are the advantages and disadvantages of this position compared to the lateral position in this patient?
16. Which nerves are most commonly missed with axillary brachial plexus block? With interscalene block?
17. What is the local anesthetic distribution following brachial plexus block above or below the clavicle?
18. What is the expected duration of brachial plexus block with 40 mL of 1.5% mepivacaine with 5 μg per mL epinephrine?
19. What is the maximum safe dose of local anesthetic for brachial plexus block?

D. Postoperative management

1. In the postanesthesia care unit, the patient complains of dyspnea. How would you evaluate and manage this?
2. On the first postoperative day, the patient complains of persistent numbness and paresthesia in the ulnar nerve distribution. What would you tell the patient? How would you manage neurologic dysfunction after brachial plexus block that persists for 1 week?

A. Medical Disease and Differential Diagnosis

A.1. What are the presenting problems in this patient?

The patient presented for urgent surgery for a proximal humeral fracture and probably has some significant internal bleeding. The patient has significant COPD, most likely secondary to his long cigarette smoking history and has a history of multiple vasovagal episodes in the past. He also has chronic hypertension.

A.2. What additional medical history would you want to obtain?

It is important to know if the patient's fall was precipitated by a vasovagal episode or if the patient simply tripped or lost footing. The patient should be questioned whether any additional trauma occurred at the time of the fall: Has the patient's history of fainting been evaluated in the past? Does the patient have any known cardiac problems?

A.3. How can testing be done to evaluate severity of the patient's vasovagal syncope (neurocardiogenic bradycardia, asystole)?

The patient's syncopal episodes can be evaluated to determine if the cause is cardiac, including electrocardiogram, echocardiogram, and exercise stress test. Electrophysiologic studies and continuous cardiac (Holter) monitoring may be useful in selected patients. Neurocardiogenic syncope can be evaluated by carotid sinus massage (if no contraindications exist) and tilt-table testing with or without addition of a β-agonist. This patient had prior evaluation that documented an abnormal response to head-up tilt-table testing during isoproterenol infusion. After the diagnosis of neurocardiogenic bradycardia, he had been maintained on oral β-blocker therapy for 20 years without further occurrence until the present episode.

Gold BS, Weitz SR, Lurie KG. Intraoperative "syncope": evaluation with tilt-table testing. *Anesthesiology*. 1992;76:635–637.

A.4. What implications does the use of atenolol have on the patient's coexisting medical condition?

The patient's use of atenolol can exacerbate COPD, especially if there is a reversible component of airway disease. However, it can be protective with regard to development of severe bradycardia or sudden asystole if the procedure is to be performed in the "beach chair" or head-up position.

A.5. Why is immobilization of the arm important following humeral fracture?

Immobilization of the arm following humeral fracture is important to avoid injury to the brachial plexus or its terminal branches.

A.6. What nerve is at particular risk for injury from humeral fracture?

The radial nerve is at particular risk, especially with midshaft humeral fracture. Following proximal humeral fracture, the shoulder can be dislocated and malpositioning can cause stretching or pressure on components of the brachial plexus. To this extent, it is important to document any pre-existing neurologic findings on examination, especially if brachial plexus block is being considered.

B. Preoperative Evaluation and Preparation

B.1. What premedication would you order?

No single premedication regimen has been shown to be consistently more effective than others. This patient has already received a recent significant intravenous dose of hydromorphone in the emergency room. If careful history rules out any significant problems or other drug intake, intravenous midazolam can be carefully titrated in the operating room while the patient is monitored with pulse oximetry in the presence of the anesthesia practitioner. Opiates should be avoided because the patient has already received intravenous hydromorphone.

B.2. What are the respiratory effects of benzodiazepines?

Although benzodiazepines almost certainly cause a dose-related, centrally mediated respiratory depression, overall respiratory depression is not nearly as profound as with the administration of intravenous opiates. Use of carefully titrated smaller therapeutic doses of midazolam is usually well tolerated, without significant respiratory depression. Use of benzodiazepines has been shown to elevate the seizure threshold during local anesthetic administration.

Arcangeli A, Antonelli M, Mignani V, Sandroni C. Sedation in PACU: the role of benzodiazepines. *Curr Drug Targets*. 2005;6:745–748.

C. Intraoperative Management

C.1. What anesthetic technique would you use?

Interscalene brachial plexus block provides excellent operating conditions and allows for postoperative analgesia.

C.2. Describe the relevant anatomy of the brachial plexus.

The brachial plexus supplies the nerves to the upper limb. It is formed by the ventral primary divisions of the fifth to the eighth cervical and the first thoracic nerves, with possible contributions from the fourth cervical and second nerve thoracic roots. The roots join to form the superior, middle, and inferior trunks, which divide into anterior and posterior divisions (Fig 45.1.) The three posterior divisions form the posterior cord, whose major branches are the radial and the axillary nerves. The upper two anterior divisions form the lateral cord, whose major branches are the musculocutaneous nerve and the lateral root of the median nerve. The lowest anterior division forms the medial cord, which gives the medial root to the median nerve and terminates as the ulnar nerve. The sympathetic contributions to the brachial plexus are derived from the middle cervical ganglion and the stellate ganglion.

The brachial plexus begins at the level of the nerve roots, usually at C5-T1. It is at this level that the interscalene brachial plexus block, first described by Winnie, is performed. Injections at this level result in a block with central characteristics, much like a one-sided neuraxial block. Resulting sensory block at this level is characterized by a dermatomal pattern. If the block is incomplete, the typical cause is inadequate spread of local anesthetic to certain nerve roots. For example, the C8-T1 nerve roots are often spared during interscalene block anesthesia because local anesthetic distribution fails to include the lower, most caudal, nerve roots of the brachial plexus. As the brachial plexus courses more peripherally from the neck to the axilla, the nerve roots transform to trunks, divisions, cords, and finally form fully differentiated peripheral nerves.

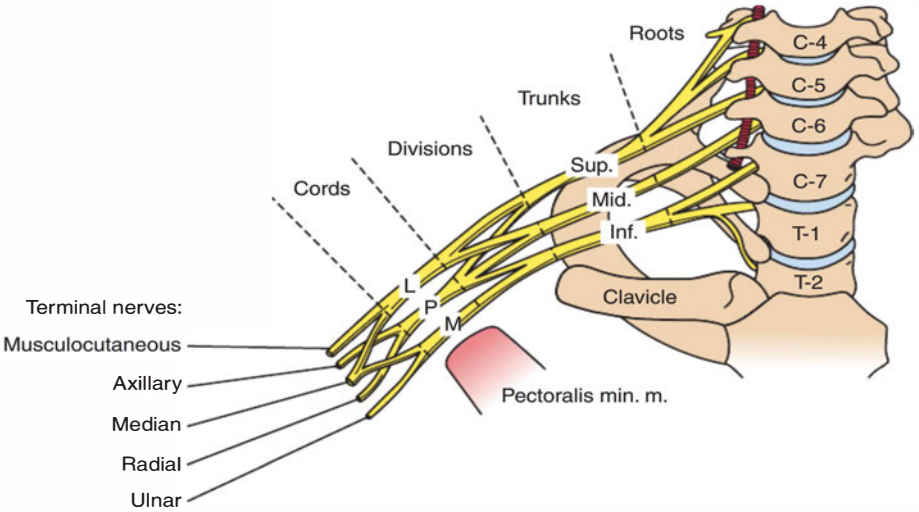


Figure 45.1 The brachial plexus. The roots join to form the superior (Sup), middle (Mid), and inferior (Inf) trunks, which divide into anterior and posterior divisions.

At the level of the axilla, where axillary block is performed, the plexus is composed of terminal nerves that include the median, radial, ulnar, and musculocutaneous nerves. At this level, an incomplete block typically spares sensory or motor blockade in the distribution of a given peripheral nerve, for example, the lateral antebrachial cutaneous nerve (the terminal sensory branch of the musculocutaneous nerve), which exits the surrounding fascia high in the brachial plexus. At this level, the nerves are spread out anatomically around the axillary artery and, depending upon the location of the needle tip during injection and the volume of local anesthetic, any of the four nerves could be spared. This has resulted in the description of multiple injection techniques for axillary block to ensure complete brachial plexus anesthesia.

At the level of the nerve roots or trunks, the brachial plexus is simply a neural plexus, being devoid of major consistently identifiable blood vessels. At this level, brachial plexus identification (i.e., needle tip location) relies on a neural response (paresthesia or motor response to electrical nerve stimulation) or direct imaging (e.g., using ultrasonographic guidance) of the neural tissue itself. At the level of the clavicle and first rib, the plexus picks up the subclavian artery, later to become the axillary artery. At this level or below, one can take advantage of the blood vessels (by palpation, Doppler flow guidance, or ultrasonographic guidance) to assist in the performance of brachial plexus block, and true perivascular techniques of brachial plexus block are the commonly preferred techniques.

Lanz E, Theiss D, Jankovic D. The extent of blockade following various techniques of brachial plexus block. *Anesth Analg*. 1983;62:55–58.

Neal JM, Gerancher JC, Hebl JR, et al. Upper extremity regional anesthesia: Essentials of our current understanding, 2008. *Reg Anesth Pain Med*. 2009;34:134–170.

Urmey W. Pulmonary complications. In: Neal JM, Rathmell J, eds. *Complications in Regional Anesthesia and Pain Medicine*. Philadelphia: Saunders; 2007:147–156.

Winnie AP. Interscalene brachial plexus block. *Anesth Analg*. 1970;49:455–466.

C.3. What relevant anatomic structures in the neck and below the neck can be injured or injected accidentally during brachial plexus block?

The brachial plexus in the neck has multiple significant anatomic relationships that include the phrenic nerve, subarachnoid space, epidural space, spinal cord, proximal nerve roots, vertebral artery, jugular veins, and the apex of the lung. Errant needle passes can hit any one of these, and in fact, there are published case reports of complications from needle injury or local anesthetic injection for each of these anatomic structures

Below the neck, the major relevant structures are the blood vessels in the neurovascular plexus, which include the subclavian artery and vein, which more distally become the axillary artery and vein, as well as the parietal pleural, visceral pleural, and lung.

C.4. What regional technique would you choose to block the brachial plexus in this patient?

Interscalene block gives the most complete block for shoulder surgery and facilitates the placement of a catheter that can be used to extend the operative anesthesia or to administer prolonged postoperative analgesia if this is desired.

C.5. What are the advantages and disadvantages of the following blocks?

a. Interscalene block
b. Subclavian perivascular block
c. Ultrasound-guided supraclavicular block
d. Ultrasound-guided infraclavicular block
e. Axillary block

a. Interscalene block

Advantages of interscalene block include a superficial location of the interscalene space that makes it easily accessible by paresthesia, nerve stimulation, or ultrasonographic guidance techniques. Injection of an adequate volume of local anesthetic at the interscalene level results in reliably complete anesthesia or analgesia for surgery on or about the shoulder, including proximal humeral surgery. A single injection results in success rates approaching 100%. A catheter can be easily placed at this site. Finally, the axillary nerve to the deltoid and the musculocutaneous nerve to the biceps brachialis derive from the C5-C6 nerve roots, and therefore reliable relaxation of the deltoid and biceps muscles is guaranteed. This allows optimal surgical exposure and facilitates dislocation of the humeral head from the glenoid socket. If performed properly, it is impossible to cause a pneumothorax with an appropriate needle using this approach.

Disadvantages include the lack of blood vessels in the interscalene space that make perivascular techniques impossible. Close proximity of the phrenic nerve, or perhaps nerve root marginalization of those fibers contributing to phrenic nerve formation, has rarely resulted in injury to these structures and reported cases of permanent phrenic nerve palsy. Interscalene block with a volume of local anesthetic adequate for surgery results in 100% incidence of ipsilateral hemidiaphragmatic paresis.

b. Subclavian perivascular block

Advantages of subclavian perivascular block include the compact plexus at this level and the subclavian artery as a landmark. The major disadvantage is the very real possibility of pneumothorax.

c. Ultrasound-guided supraclavicular block

Advantages of ultrasound-guided supraclavicular block include superficial location of the artery and plexus that allow for easy imaging and perivascular blockade. Also, one is able to visualize two-dimensional local anesthetic distribution and can avoid inadvertent puncture or injection into the vessels. Disadvantages include the intimate

proximity to the apex of the lung, which has resulted in case reports of pneumothorax following this block. In addition, as with all ultrasound-guided blocks, larger gauged needles are often preferred to enhance imaging, which may theoretically cause more trauma than smaller gauge needles used for conventional techniques. Supraclavicular block is associated with a significant incidence of diaphragmatic paresis.

d. Ultrasound-guided infraclavicular block

Advantages of infraclavicular block include the artery, which facilitates imaging for perivascular brachial plexus block. The block does not require positioning of the upper extremity. It is easy to place a catheter at a central location of the plexus via this approach. Disadvantages are related to the depth of the plexus at this level. This may cause more discomfort and is best performed using a curvilinear probe of lower frequency, employing an in-plane technique. The depth results in poor image quality of the distal shaft and tip of the needle.

e. Axillary block

The axillary block is characterized by the major advantage of the superficial location of the individual terminal branches of the brachial plexus. Thus, one can target the fully differentiated terminal nerves by using either nerve stimulation or paresthesia techniques. Disadvantages include the need to locate more than one nerve to guarantee successful brachial plexus block at this level. In addition, as with infraclavicular block, the musculocutaneous nerve is missed with a high frequency.

Chan V. *Ultrasound Imagery for Regional Anesthesia: A Practical Guide*. 2nd ed. Toronto: VW Chan; 2009:47–59

Knoblanche GE. The incidence and aetiology of phrenic nerve blockade associated with supraclavicular brachial plexus block. *Anaesth Intensive Care*. 1979;7:346–349.

Macfarlane AJ, Perlas A, Chan V, Brull R. Eight ball, corner pocket ultrasound-guided supraclavicular block: avoiding a scratch. *Reg Anesth Pain Med*. 2008;33:502–503; author reply 504.

Neal JM, Moore JM, Kopacz DJ, et al. Quantitative analysis of respiratory, motor, and sensory function after supraclavicular block. *Anesth Analg*. 1998;86:1239–1244.

Soares LG, Brull R, Lai J, Chan VW. Eight ball, corner pocket: the optimal needle position for ultrasound-guided supraclavicular block. *Reg Anesth Pain Med*. 2007;32:94–95.

Urmey W. Pulmonary complications. In: Neal JM, Rathmell J, eds. *Complications in Regional Anesthesia and Pain Medicine*. Philadelphia: Saunders; 2007:147–156.

C.6. Describe landmarks and procedures for interscalene block with nerve stimulation and ultrasound.

For interscalene block by electrical nerve stimulation, the patient's head is turned away from the side of the block at an approximately 45-degree angle with the surface of the bed or table. The interscalene groove (between the anterior and middle scalene muscles) is located by palpation just posterior to the lateral border of the sternocleidomastoid muscle. The electrically shielded stimulating needle is introduced in a dorsal, medial, and caudal direction until an appropriate motor response is elicited. Because of the orientation of the nerve roots in a cephalocaudad plane, a response from C5-C6 nerve roots is most frequently obtained first. C5-C6 motor response is characterized by deltoid, biceps, or brachioradialis muscle contractions. Reduction of electrical current amplitude below 0.5 mAmp at a pulse duration of 0.1 ms results in a success rate with single injection close to 100%.

For interscalene block by ultrasonographic guidance, either an in-plane or out-of-plane approach can be used, depending on the experience and preference of the operator. For an in-plane approach, the needle is inserted in a posterolateral to

anteromedial direction along the long axis of a high-frequency linear array transducer with the needle shaft and tip visualized. The middle and anterior scalene muscles should be visualized, and the hypoechoic nerve roots are usually stacked in a somewhat cephalocaudad arrangement. Injection should be made so that real-time spread of anesthetic can be visualized within the brachial plexus sheath spreading the cross-sectional nerve roots apart.

For an out-of-plane approach (Fig. 45.2), the high-frequency linear array transducer may be placed just caudal to the conventional interscalene block injection point and just above the clavicle. The longitudinal axis of the transducer is oriented in a posterolateral to anteromedial direction, with the center of the probe overlying the interscalene space and the image of the nerve roots, which again will be hypoechoic in cross-section. The needle is introduced in a slightly dorsal, medial, and caudal direction, as originally described in the conventional technique by Winnie. Nerve stimulation can be used to confirm position of the needle tip in the brachial plexus.

Chan V. *Ultrasound Imagery for Regional Anesthesia: A Practical Guide*. 2nd ed. Toronto: VW Chan; 2009:47–59.

Kapral S, Greher M, Huber G, et al. Ultrasonographic guidance improves the success rate of interscalene brachial plexus blockade. *Reg Anesth Pain Med*. 2008;33:253–258.

Perlas A, Chan V. Ultrasound-assisted nerve blocks in adults. In: Hadzic A, ed. *Textbook of Regional Anesthesia and Acute Pain Management*. New York: McGraw Hill, 2007: 663–672.

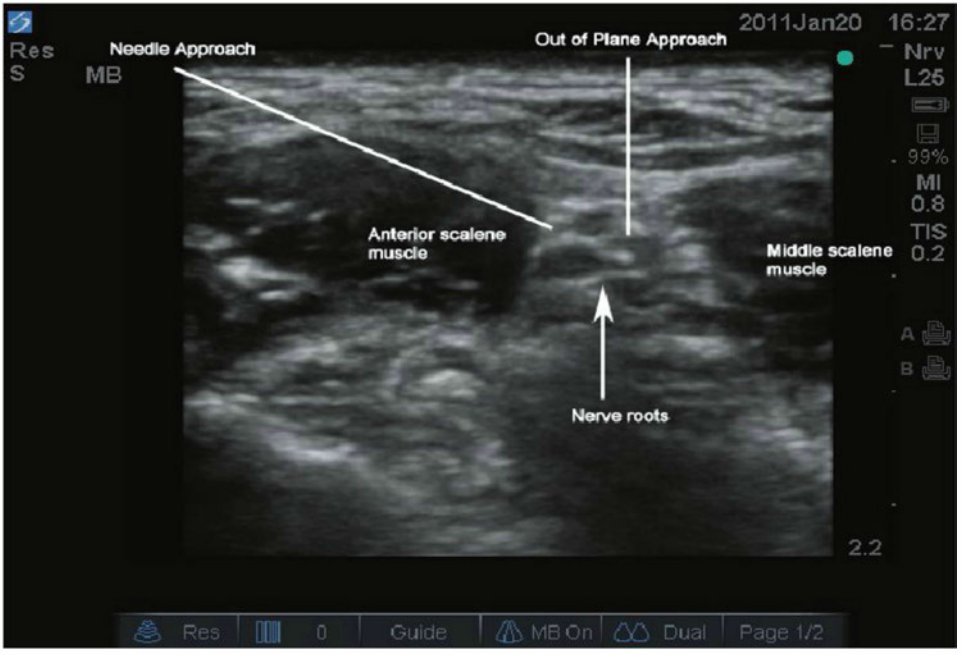


Figure 45.2 Ultrasonograhic (U/S) guidance for interscalene block. Hypoechoic roots can be visualized between the anterior and middle scalene muscles. Plexus may be reached and injected via either A, in-plane approach, or B, out-of-plane approach. Dual guidance utilizing a nerve stimulator in conjunction with U/S is easily applied at this level of the brachial plexus.

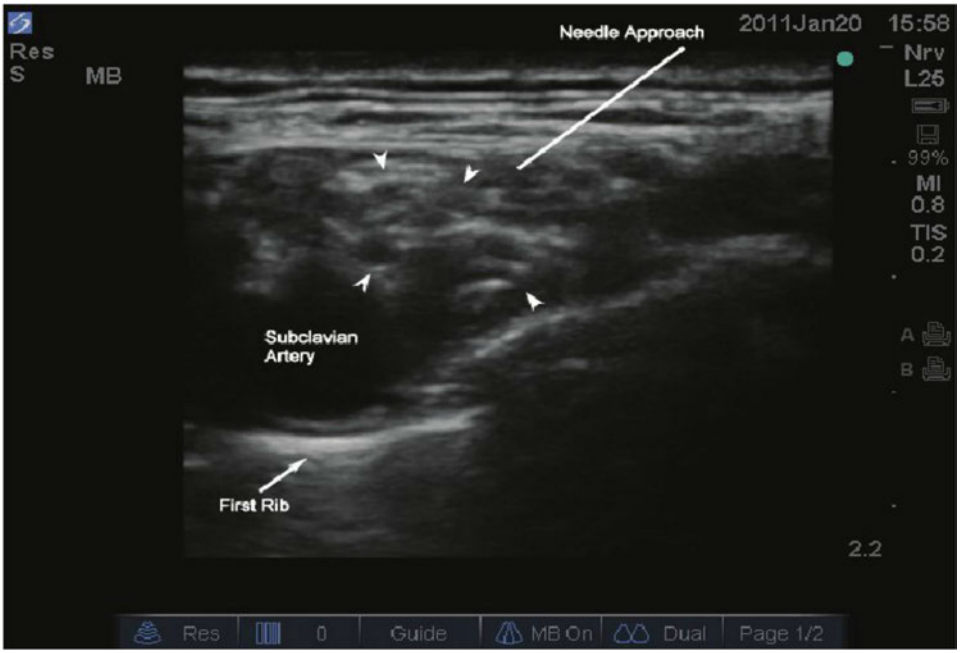


Figure 45.3 Supraclavicular nerve block guided by ultrasound.

C.7. Describe landmarks and procedures for ultrasound-guided supraclavicular block.

The brachial plexus in the supraclavicular area is located posterolateral to the subclavian artery. The plexus is above the first rib, which can be imaged. A high-frequency linear array transducer is placed just above and parallel to the clavicle in the supraclavicular fossa (Fig. 45.3.). An in-plane posterolateral to anteromedial technique is used, making sure that the needle tip and shaft are visualized throughout manipulation of the needle and that the pleura is clearly seen. Local anesthetic is deposited in more than one location among the trunks/divisions of the brachial plexus.

C.8. Describe landmarks and procedure for ultrasound-guided infraclavicular block.

The ultrasound-guided infraclavicular block is usually performed by an in-plane approach with a lower frequency curvilinear transducer that is positioned in the deltopectoral groove. This can be a relatively deep block, and it may require a needle of up to 10 cm in length. The axillary artery and vein and cords of the brachial plexus are visualized (Fig. 45.4). The needle is placed just cephalad to the center of the long axis of the probe and inserted at an angle of 45 degrees until the tip encounters the brachial plexus. This is a perivascular block, and the arterial pulsations greatly facilitate ability to use an out-of-plane approach effectively. One should ensure that local anesthetic spread is visible upon injection. This enhances success and helps to makes certain that accidental intravascular injection is avoided. It is preferable to deposit local anesthetic posterior to the axillary artery close to the posterior cord. It may be necessary to inject in more than one place in the brachial plexus by moving the needle around and dividing doses of local anesthetic injectate.

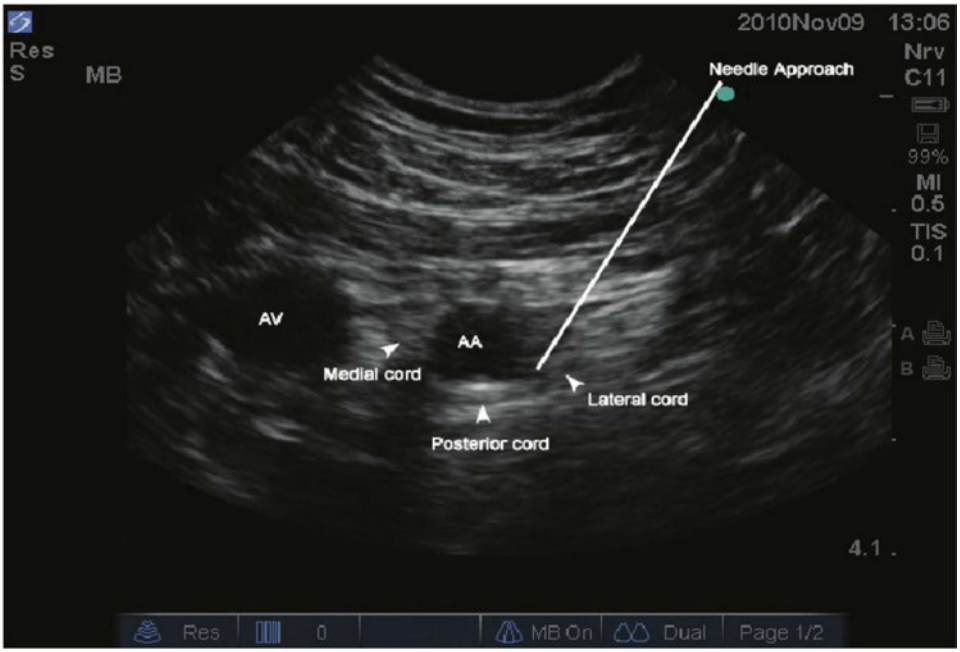


Figure 45.4 Infraclavicular nerve block guided by ultrasound.

C.9. Describe landmarks and procedure for axillary brachial plexus block using a nerve stimulator.

With the patient in a supine position, the arm is elevated to 90 degrees. The patient's artery is palpated, and a small-gauge electrically shielded stimulating needle is introduced just below the artery to elicit motor response from the radial nerve (deep to the artery) or ulnar nerve (medial to the artery; i.e., immediately below with the arm in this position). The needle is re-sited and advanced superficial to the artery for a median nerve motor response. Highest success rate correlates with at least two motor responses in which one response is from radial nerve stimulation. By insisting on current amplitude levels of 0.5 mAmps or below, at short pulse duration (0.1 msec), success rates in the 95% to 100% range can be expected.

C.10. The patient requests to have the interscalene block performed after you administer general anesthesia. Would you agree to this request?

In a landmark publication, Benumof reported four cases of permanent injury to the cervical spinal cord resulting from interscalene block performed during general anesthesia. Imaging of the cervical spinal cord showed vacuolization of the cord or the presence of a syrinx. Intraneural injection of local anesthetic under pressure has been found to spread along the longitudinal axis along the nerve during experimental studies. Thus, theoretically, injection into a proximal nerve root can spread and disrupt the cervical spinal cord.

Performance of interscalene block in the anesthetized patient does not allow the patient to report painful paresthesia or other sensations. Sudden severe pain on injection during peripheral nerve block is a time-honored signal that neural tissue is endangered and that the needle should be promptly withdrawn and re-sited. It has

been shown that needle contact with the nerve is often not associated with the ability to elicit a motor response during electrical stimulation. Reports of accidental intraneural injection during ultrasonographic needle guidance have been published. Therefore, no available modality can ensure against this devastating complication. It is strongly advised that interscalene block not be performed in a patient who is heavily sedated or following induction of general anesthesia.

Auroy Y, Benhamou D, Bargues L, et al. Major complications of regional anesthesia in France. The SOS regional anesthesia hotline service. *Anesthesiology*. 2002;97:1274–1280.

Benumof J. Permanent loss of cervical spinal cord function associated with interscalene block performed under general anesthesia (case report). *Anesthesiology*. 2000;93:1541–1544.

Bromage P. Nerve injury and paralysis related to spinal and epidural anesthesia. *Reg Anesth*. 1993;18:481–484.

Hadzic A, Dilberovic F, Shah S, et al. Combination of intraneural injection and high injection pressure leads to fascicular injury and neurologic deficits in dogs. *Reg Anesth Pain Med*. 2004;29:417–423.

Urmey W, Stanton J. Inability to consistently elicit a motor response following sensory paresthesia during interscalene block administration. *Anesthesiology*. 2002;96:552–554.

C.11. What relevant respiratory complications or side effects are you concerned about in this patient?

Ipsilateral hemidiaphragmatic paresis is a consistent side effect associated with interscalene block. It occurs with an incidence of 100%. This expected side effect takes on added importance if the patient has respiratory comorbidities, including contralateral phrenic or diaphragmatic pathology, severe chronic obstructive cardiopulmonary disease, neuromuscular disorders in which a 25% reduction in FVC would not be tolerated, or conditions that restrict ribcage motion such as ankylosing spondylitis. If these conditions are present, significant atelectasis or respiratory failure can occur. With proper technique and needle size, there is no possibility of causing a pneumothorax. Introduction of a catheter, nevertheless, could theoretically reach the apex of the lung.

Urmey W, Talts K, Sharrock N. One hundred percent incidence of hemidiaphragmatic paresis associated with interscalene brachial plexus anesthesia as diagnosed by ultrasonography. *Anesth Analg*. 1991;72:498–503.

C.12. What is the incidence of hemidiaphragmatic paresis following interscalene brachial plexus block? Can this complication be avoided by lowering the volume or concentration of local anesthetic injected? By using ultrasound-guided supraclavicular block?

Hemidiaphragmatic paresis occurs 100% of the time with interscalene block and cannot be avoided by reducing the volume of local anesthetic injected. Volumes as low as 5 mL (which is inadequate for surgical anesthesia) have been associated with a 45% incidence of hemidiaphragmatic paresis. Similarly, reductions in local anesthetic concentration do not avoid this side effect, with concentrations of bupivacaine as low as 0.125% being associated with 100% incidence of hemidiaphragmatic paresis. The use of ultrasound-guided supraclavicular blocks may reduce the incidence of hemidiaphragmatic paresis from 100%, but will still be expected to be associated with a significant incidence. Blocks above the clavicle are associated with spread of local anesthetic into the cervical plexus. The mechanism for phrenic nerve paresis is motor blockade of the C3-C5 nerve roots before forming the phrenic nerve. The main nerve root contributing to formation to the

phrenic nerve is the C4 nerve root. Any block causing sensory blockade of C5, C4, or C3 would be expected to have associated phrenic paresis. A recent publication suggests that with careful deposition of local anesthetic by ultrasonographic guidance, the incidence of hemidiaphragmatic paresis may indeed be avoided during supraclavicular block.

Renes SH, Spoormans HH, Gielen MJ, et al. Hemidiaphragmatic paresis can be avoided in ultrasound-guided supraclavicular brachial plexus block. *Reg Anesth Pain Med*. 2009;34:595–599.

Sinha S, Abrams J, Barnett J, et al. Decreasing the local anesthetic volume from 20 to 10 mL for ultrasound-guided interscalene block at the cricoid level does not reduce the incidence of hemidiaphragmatic paresis. *Reg Anesth Pain Med*. 2011;36:17–20.

Urmey W, Gloeggler P. Pulmonary function changes during interscalene block: effects of decreasing local anesthetic injection volume. *Reg Anesth*. 1993;18:244–249.

Urmey W, Talts K, Sharrock N. One hundred percent incidence of hemidiaphragmatic paresis associated with interscalene brachial plexus anesthesia as diagnosed by ultrasonography. *Anesth Analg*. 1991;72:498–503.

C.13. Describe the pulmonary function changes that occur after interscalene brachial plexus block.

Pulmonary function (such as FVC and forced expiratory volume in 1 second) reductions of 25% to 30% occur routinely. These changes are usually complete within 15 minutes of completion of the injection. Increased upper rib cage expansion and ipsilateral paradoxical inward motion of the hemiabdomen have been reported (Fig. 45.5). The combined effect of these changes is a reduced ability to cough and clear secretions, which may be poorly tolerated by a patient with severe COPD.

Urmey W, McDonald M. Hemidiaphragmatic paresis during interscalene brachial plexus block: effects on pulmonary function and chest wall mechanics. *Anesth Analg*. 1992;74:352–357.

C.14. What would you do if the patient complained of dyspnea after you performed an interscalene block?

The patient should be reassured and observed. Most patients complaining of dyspnea will have more than adequate pulmonary function for normal respiration. Symptoms of dyspnea may be relieved by placing the patient in the upright or sitting position as tolerated. This position optimizes diaphragmatic geometry and function and increases functional residual capacity. Auscultation often reveals diminished or silent breath sounds on the side of the block. Chest radiography may be obtained if pneumothorax is suspected. Application of a face mask to assess ventilation or end-tidal carbon dioxide may be done, and assisted or controlled ventilation can be used if necessary. Endotracheal intubation should be performed if clinically indicated.

C.15. The surgeon prefers to perform the surgical procedure in the sitting position. What are the advantages and disadvantages of this position compared to the lateral position in this patient?

As discussed earlier, the seated position optimizes chest wall mechanics. However, placing the patient in the seated position may be associated with hypotension or bradycardia. Severe bradycardia or asystole may occur. It is suggested that these events occur as a result of the Bezold-Jarisch reflex (paradoxical cardiac inhibition and bradycardia in response to decreased ventricular volume resulting from venous pooling in sitting position). Use of intravenous β-blockers may help to diminish the incidence

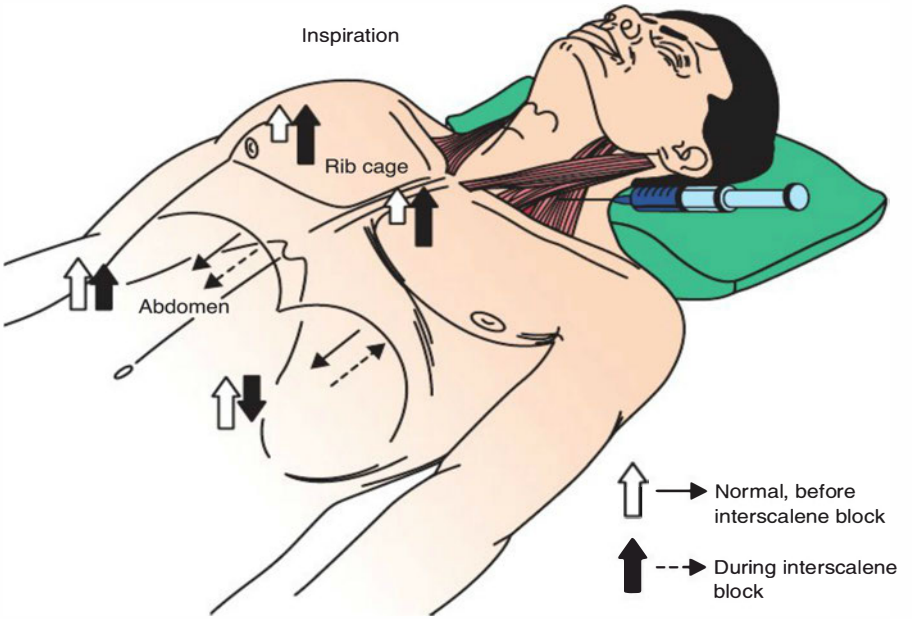


Figure 45.5 Illustration of typical changes in chest wall motion measured by magnetometry during interscalene anesthesia. The ipsilateral hemiabdomen no longer expanded, contracting instead with tidal inspiration 10 minutes after interscalene brachial plexus injection of mepivacaine. (From Urmey WF, McDonald M. Hemidiaphragmatic paresis during interscalene brachial plexus block: effects on pulmonary function and chest wall mechanics. *Anesth Analg*. 1992;74:356, with permission.)

of significant hypotension and bradycardia. The sitting position may be thought of as a variation of the tilt-table test. This patient would be at particular risk for developing intraoperative bradycardia in the sitting position because of the history of syncopal episodes and positive findings on the tilt test. Intraoperative bradycardia can be easily treated with small doses of intravenous epinephrine, ephedrine, atropine, and intravenous fluids. Vigilance and rapid response are of critical importance.

Gold BS, Weitz SR, Lurie KG. Intraoperative "syncope": evaluation with tilt-table testing. *Anesthesiology*. 1992;76:635–637.

Kahn RL, Hargett MJ. Beta-adrenergic blockers and vasovagal episodes during shoulder surgery in the sitting position under interscalene block. *Anesth Analg*. 1999;88:378–381.

Liguori GA, Kahn RL, Gordon J, et al. The use of metoprolol and glycopyrrolate to prevent hypotensive/bradycardic events during shoulder arthroscopy in the sitting position under interscalene block. *Anesth Analg*. 1998;87:1320–1325.

Tarkkila P, Isola J. A regression model for identifying patients at high risk of hypotension, bradycardia and nausea during spinal anesthesia. *Acta Anaesthesiol Scand*. 1992;36:554–558.

C.16. Which nerves are most commonly missed with axillary brachial plexus block? With interscalene block?

Axillary brachial plexus block commonly misses the musculocutaneous nerve, which arises from C5-C6 nerve roots and exits the plexus above the axilla. Interscalene block

commonly spares the ulnar nerve, which is formed by the C8-T1 nerve roots at the lower extent of the brachial plexus.

Lanz E, Theiss D, Jankovic D. The extent of blockade following various techniques of brachial plexus block. *Anesthesia & Analgesia*. 1983;62:55–58.

C.17. What is the local anesthetic distribution following brachial plexus block above or below the clavicle?

The brachial plexus can be thought of as a structure that is enclosed by fascia to form an hourglass-shaped anatomic compartment. The upper chamber of the hourglass is a flattened triangular space containing the nerve roots and trunks of the brachial plexus, which are stacked in a plane. Below the clavicle, a more conventional three-dimensional cylindrical lower hourglass chamber shape applies, widening as the plexus courses distally away from the impingement point, which is at the level of the junction of the clavicle and first rib (where the divisions are located). Clinically, the shape of each compartment, and particularly the high resistance at the middle of the "hourglass" results in very different distributions of local anesthetic when injections are made above versus below the clavicle. Above the clavicle, injections result in central neuraxial block characteristics, with resulting dermatomal patterns of sensory block. Neural structures are relatively compact, and therefore small volumes are adequate to fill the sheath above the clavicle and injectate extends into the cervical plexus. Below the clavicle, the plexus is a neurovascular plexus with fully differentiated cords progressing to terminal nerves that surround the artery in a more three-dimensional anatomy. Typically, larger volumes or multiple injections are required for successful block and injections do not reach the cervical plexus.

Urmey WF. Using the nerve stimulator for peripheral or plexus nerve blocks. *Minerva Anestesiol*. 2006;72:467–471.

C.18. What is the expected duration of brachial plexus block with 40 mL of 1.5% mepivacaine with 5 μg per mL epinephrine?

Such an injection typically lasts 4 to 5 hours for surgical anesthesia.

C.19. What is the maximum safe dose of local anesthetic for brachial plexus block?

There is no absolute maximum safe dose of local anesthetic. The brachial plexus is characterized by relatively low systemic absorption compared to that of other blocks, such as epidural or intercostal. Absorption of local anesthetic following regional anesthetic injection is site specific. The American Society of Regional Anesthesia has published guidelines for local anesthetic toxicity. One should be cognizant of the recent publications demonstrating the efficacy of intravenous infusion of lipid emulsion in reversing local anesthetic–induced cardiac toxicity in animals and in multiple case reports involving human patients. Background information as well as advice concerning resuscitation equipment and procedure, including recommended dosing of lipid emulsion, can be obtained by accessing www.lipidrescue.squarespace.com.

Neal JM, Bernards CM, Butterworth JF, et al. ASRA practice advisory on local anesthetic systemic toxicity. *Reg Anesth Pain Med*. 2010;35:152–161.

Rosenberg PH, Veering BT, Urmey WF. Maximum recommended doses of local anesthetics: a multifactorial concept. *Reg Anesth Pain Med*. 2004;29:564–575; discussion 524.

D. Postoperative Management

D.1. In the postanesthesia care unit, the patient complains of dyspnea. How would you evaluate and manage this?

The patient's vital signs should be monitored, including the oxygen saturation. Duration of hemidiaphragmatic paresis following brachial plexus block with mepivacaine or bupivacaine with added epinephrine lasts 3 to 4 hours or 9 to 18 hours, respectively. If a catheter has been placed, it should be checked via imaging to ascertain that it is not in the cervical plexus. Chest radiography should be performed to rule out pneumothorax or significant atelectasis. The patient should be supported by placement into the sitting position and ventilation assisted or controlled if necessary.

Urmey W, Gloeggler P. Effects of bupivacaine 0.5% compared with mepivacaine 1.5% used for interscalene brachial plexus block (abstract). *Reg Anesth*. 1992;17:13.

D.2. On the first postoperative day, the patient complains of persistent numbness and paresthesia in the ulnar nerve distribution. What would you tell the patient? How you would you manage neurologic dysfunction after brachial plexus block that persists for 1 week?

Brachial plexus block via the interscalene approach is characterized by sparing of the C8-T1 nerve roots (ulnar distribution) approximately 50% of the time, even with an injectate volume of 50 mL local anesthetic. The needle does not contact the C8-T1 nerve roots, and therefore direct injury would be exceedingly rare following interscalene block. More commonly, short-term ulnar neuropathy occurs from intraoperative positioning, including pressure at the elbow, flexion at the elbow, or dislocation of the humeral head during open shoulder surgery. Use of a pneumatic tourniquet can also result in such neuropathy. I would tell the patient that this typically goes away after a short period and that if it persists for 1 week, a neurologist would be contacted to evaluate the possibility of ulnar neuropathy or brachial plexopathy. Even persistent neuropathy typically resolves completely in 3 to 6 months. Electromyography can be performed to ascertain the site of any lesion and whether it is at the level of the brachial plexus.

Borgeat A, Ekatodramis G, Kalberer F, Benz C. Acute and nonacute complications associated with interscalene block and shoulder surgery: a prospective study. *Anesthesiology*. 2001;95:875–880.

Bromage P. Nerve injury and paralysis related to spinal and epidural anesthesia. *Reg Anesth*. 1993;18:481–484.

Liguori GA, Zayas VM, Yadeau JT, Kahn RL, Paroli L, Buschiazzo V, Wu A. Nerve localization techniques for interscalene brachial plexus blockade: a prospective, randomized comparison of mechanical paresthesia versus electrical stimulation. *Anesthesia & Analgesia*. 2006;103:761–767.

CHAPTER 46

Nerve Blocks of the Lower Extremity

Jeffrey Y. F. Ngeow, David Wang, and Karina Gritsenko

A 67-YEAR-OLD MAN

is scheduled for exploration of a displaced right metatarsal fracture after stumbling on a carpet. His medical history is significant for stage III multiple myeloma, osteoporosis, anemia, increased cholesterol, and chronic back pain related to prior pathologic compression fractures. The patient recently completed a course of chemotherapy and radiation for refractory myeloma. Regular medications include aspirin 81 mg, atorvastatin, OxyContin 10 mg three times daily, oxycodone 15 mg 1 or 2 tablets every 4 to 6 hours as needed, pregabalin 100 mg twice daily, and bisphosphonates. Foot radiographs show spiral fracture of the right fifth metatarsus. Previous magnetic resonance imaging (MRI) showed multiple lumbar compression fractures and degenerative disease without compression of the spinal cord. The patient's hemoglobin is 7.2 g per dL, calcium level is 13.1 mg per dL, and platelets count 79 $\times$ 10^3 per μL. Prior anesthetic records yielded a history of difficult intubations.

A. Medical Disease and Differential Diagnosis

1. What is multiple myeloma?
2. What are concerns associated with multiple myeloma?
3. What is the significance of a pathologic fracture?
4. What is the significance of hypercalcemia and thrombocytopenia in this patient?

B. Preoperative Evaluation and Preparation

1. Will you be concerned with the status of neurologic function in this patient?
2. What is the significance of the abnormal MRI findings?
3. What other investigations should be reviewed in evaluating this patient?
4. Should one proceed with surgery at this time?

5. What anesthetic options should be discussed with the patient preoperatively?
6. What special concerns exist related to neuraxial anesthesia in this patient?

C. Intraoperative Management

1. What special monitoring should be employed intraoperatively?
2. Which peripheral nerve blocks can be used for exploration of the metatarsals? What are the landmarks for an ankle block?
3. What are the advantages and disadvantages of an ankle block?
4. What other peripheral regional anesthetic techniques may be appropriate?
5. How is ultrasound guidance useful in performing peripheral nerve blocks?
6. What are the risks of peripheral nerve block in an immune-compromised patient?

D. Postoperative Management

1. How should the postoperative pain be managed in this patient?
2. Why should the neurovascular status of the foot be followed?

E. Summary

A. Medical Disease and Differential Diagnosis

A.1. What is multiple myeloma?

Multiple myeloma is a disease characterized by proliferation of malignant plasma cells and subsequent overabundance of monoclonal paraprotein. These collections of abnormal cells can accumulate in the bone marrow and interfere with production of normal cells. The monoclonal paraprotein can also interfere with kidney functions and alter the production of normal antibodies. Results of this disease include renal failure, immunodeficiency, infection, hypercalcemia, anemia, weakness, confusion, and fatigue.

Fauci AS, Braunwald E, Kasper DL, et al., eds. *Harrison's Principles of Internal Medicine*. 17th ed. New York: McGraw-Hill; 2008:701–706.

Ross JS, Brant-Zawadzki M, Moore KR, et al. eds. *Diagnostic Imaging Spine*. 1st ed. Salt Lake City: Amirsys; 2005:66–69.

A.2. What are concerns associated with multiple myeloma?

Specific concerns related to multiple myeloma include bone pain, bone metastases, pathologic fractures, spinal cord compression, renal dysfunction, hypercalcemia, leukopenia, anemia, and abnormal bleeding from thrombocytopenia. In addition, the aberrant antibodies may lead to impairment of normal humoral immunity, increasing the patient's susceptibility to encapsulated organisms.

Fauci AS, Braunwald E, Kasper DL, et al., eds. *Harrison's Principles of Internal Medicine*. 17th ed. New York: McGraw-Hill; 2008:701–706.

A.3. What is the significance of a pathologic fracture?

Pathologic fractures are secondary to bone lesions, which include infections and tumor, such as metastases, lymphoma, plasmacytoma, bone cysts, lipoma, and osteoblastoma. These bone lesions can occur in multiple sites of the body. Up to 93% of

myeloma patients have more than one site of bone involvement. A severe bone event is a common presentation in this patient group.

Specifically bone-related pain is the most common symptom of multiple myeloma. It is the most common cancer to metastasize to bone, with up to 90% of patients developing bone lesions and 60% of patients developing a pathologic fracture over the course of their disease. Persistant localized pain is typical of a pathologic fracture in this patient population.

Esteve FR, Roodman GD. Pathophysiology of myeloma bone disease. *Best Pract Res Clin Haematol*. 2007;20:613–624.

Fauci AS, Braunwald E, Kasper DL, et al., eds. *Harrison's Principles of Internal Medicine*. 17th ed. New York: McGraw-Hill; 2008:701–706.

A.4. What is the significance of hypercalcemia and thrombocytopenia in this patient?

Significant laboratory abnormalities in this patient may indicate a patient having lytic lesions, compression fractures, or renal insufficiency. Multiple myeloma can affect the production and inhibition of one or more clotting factors or have an additive effect with other cancers with paraprotein disorders, particularly primary or metastatic liver cancer. The chemotherapy that is used to treat malignancies may also cause such changes. These features may affect the choice of anesthesia technique or anesthetic dosing (renal versus hepatic metabolism of a medication in a patient with an elevated creatinine).

Grethlein SJ, Thomas LM. Multiple Myeloma. *EMedicine*. Available at: http://emedicine.medscape.com/article/204369-overview. Accessed December 8, 2010.

Horlocker TT, Wedel DJ. Regional anesthesia in the immunocompromised patient. *Reg Anesth Pain Med*. 2006;31:334–345.

B. Preoperative Evaluation and Preparation

B.1. Will you be concerned with the status of neurologic function in this patient?

In this patient with a history of malignancy and pathologic fractures, one must consider possible nerve injury from compression or invasion. Furthermore, given that the patient is currently thrombocytopenic, the risk for surgery-related hematoma and subsequent nerve damage is increased. As part of the preoperative evaluation, a thorough physical examination including a complete neurologic assessment of strength and sensory testing should be recorded before performing any regional anesthesia.

Hines RL, Greene NM, eds. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Saunders; 2008:516–517.

B.2. What is the significance of the abnormal MRI findings?

Given the patient's history of chronic low back pain and multiple compression fractures, one would expect increased technical difficulty in placing a neuraxial anesthetic.

In addition, trauma from needling may increase the risk for spinal hematoma. Any invasive procedure along the spine might cause additional pain.

Mahnken AH, Wildberger JE, Gehbauer G, et al. Multidetector CT of the spine in multiple myeloma: comparison with MR imaging and radiography. *AJR Am J Roentgenol*. 2002;178:1429–1436.

Ross JS, Brant-Zawadzki M, Moore KR, et al., eds. *Diagnostic Imaging Spine*. 1st ed. Salt Lake City: Amirsys; 2005:66–69.

B.3. What other investigations should be reviewed in evaluating this patient?

Preoperative workup in this patient should include a review of the chest and foot radiographs, laboratory values including biochemistry, electrolytes, and the coagulation profile.

Foot radiography will show the extent of the fracture and guide the type of regional anesthesia selected. For example, if bone grafting seems necessary, it will certainly need to be considered in the anesthetic plan.

A chest radiograph may show lung metastases and even pericardial effusions in a patient with disseminated cancer. Such findings may have a bearing on intraoperative management and postoperative analgesic requirements.

Biochemistry test results will help to rule out systemic conditions that could be expected in a patient with progressive multiple myeloma, including hypercalcemia and renal insufficiency. In addition, one must also be alert to bleeding concerns resulting from thrombocytopenia, platelet dysfunction, and compromised immune status in patients with recent chemotherapy.

Grethlein SJ, Thomas LM. Multiple Myeloma. *EMedicine*. Available at: http://emedicine.medscape.com/article/204369-overview. Accessed December 8, 2010.

B.4. Should one proceed with surgery at this time?

Based on the laboratory values, the patient has a notable hypercalcemia that could be indicative of other abnormalities such as renal dysfunction, hyperviscosity, or hypovolemia. In this scenario, the operation being an elective procedure, it would be appropriate to correct any electrolyte abnormality before proceeding to the operating room.

Grethlein SJ, Thomas LM. Multiple Myeloma. *EMedicine*. Available at: http://emedicine.medscape.com/article/204369-overview. Accessed December 8, 2010.

Hines RL, Greene NM, eds. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Saunders; 2008:516–517.

B.5. What anesthetic options should be discussed with the patient preoperatively?

The most simple and safe anesthetic approach that is compatible with the requirements of the surgery and is acceptable to the patient should be used. In this case study, the history of difficult intubation makes general anesthesia a less desirable option for peripheral surgery. The use of neuraxial techniques is also less desirable given the current thrombocytopenia, history of pathologic fractures, and possible tumor within the spine.

Actual risk for vertebral canal (spinal) hematoma in a patient with thrombocytopenia is unclear. There are even fewer data on the safety of peripheral nerve blocks in the presence of thrombocytopenia. All of the major bleeding complications associated with anticoagulation and nonneuraxial regional techniques that have been reported in the literature occurred after psoas compartment or lumbar sympathetic nerve blocks. Case reports suggest that the major risk of nerve blocks in the presence of anticoagulation relates to blood loss, rather than neurologic complications. If surgery is deemed urgent by the surgeon, a reasonable anesthetic plan may include performing an ankle block for the foot and another peripheral nerve block for the iliac crest, in anticipation of the need for bone graft harvesting.

The mention of nerve blocks may evoke fear of painful needles and anxiety at the possibility of intraoperative pain or awareness. A full discussion of the risks and benefits of any regional anesthetic technique is an important part of the preoperative anesthetic consultation. Irrespective of the anesthetic techniques selected, the patient must be assured of adequate relief from anxiety and pain during the induction of anesthesia, the operation itself, and the postoperative period.

There should also be a discussion of the nature and possible side effects of the drugs involved, including the medications used for intraoperative sedation, as well as the local anesthetic agents. The patient should be informed that regardless of the anesthetic technique used, neither complete anesthesia nor amnesia can be ensured at all stages of the operation.

Shah S, Tsai T, Iwata T, et al. Outpatient regional anesthesia for foot and ankle surgery. *Int Anesthesiol Clin.* 2005;43:143–151.

Spitellie PH. Holmes MA. Domino KB. Awareness during anesthesia. *Anesthesiol Clin North America*. 2002;20:555–570.

B.6. What special concerns exist related to neuraxial anesthesia in this patient?

Issues with coagulopathy can be of significant concern in patients with cancer. Bone marrow replacement by tumor or suppression by chemotherapy can cause thrombocytopenia, hypofibrinogenemia, prolonged prothrombin, thrombin, activated partial thromboplastin times, and elevated fibrinogen degradation products. All of them create higher risks for spinal hematoma. In addition, patients with cancer have a sixfold increase in risk for developing thromboembolism or even disseminated intravascular coagulopathy; thus, pharmacologic prophylaxis with heparin, low molecular weight heparin, or warfarin can be appropriate. If this patient had a history of requiring anticoagulation, the anesthetic technique would be influenced by the timing of the anticoagulant given, especially if a neuraxial anesthetic is chosen.

In patients with a higher likelihood of bone metastases such as cancer of the breast, lung, prostate, or multiple myeloma, the vertebral column is often involved. There has been some concern regarding neuraxial anesthesia and catheter placement, for example, in patients with acute lymphoblastic leukemia. It was thought that traumatic or bloody puncture of the dura may seed the spine with blast cells and thus worsen outcome. At this time, the evidence to support this is sparse and the American Society of Regional Anesthesia (ASRA) guidelines contain no clear recommendation for or against it.

Ayerbe J, Quinones D, Prieto E, et al. Spinal subarachnoid hematoma after lumbar puncture in a patient with leukemia: report of a case and review of the literature [Spanish]. *Neurocirugia*. 2005;16:447–452.

Horlocker TT, Wedel DJ. Regional anesthesia in the immunocompromised patient. *Reg Anesth Pain Med.* 2006;31:334–345.

Horlocker TT, Wedel DJ, Rowlingson JC, et al. *Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy: american society of regional anesthesia and pain medicine evidence-based guidelines.* 3rd ed. *Reg Anesth Pain Med.* 2010;35:64–101.

Howard SC, Gajjar AJ, Cheng C, et al. Risk factors for traumatic and bloody lumbar puncture in children with acute lymphoblastic leukemia. *JAMA.* 2002;288:2001–2007.

C. Intraoperative Management

C.1. What special monitoring should be employed intraoperatively?

Special monitoring in this case may include a Doppler ultrasound flow detector probe on the operated limb before and after induction of anesthesia. In most cases, an increase in blood flow occurs after successful neural blockade. Any change, or lack of change, in the perfusion status of the foot should be documented. When continuous intraoperative blood flow monitoring is necessary, a sterile probe for pulse oximetry with plethysmographic display may be attached to a nearby digit, if the operating condition permits. If a tourniquet is required, which is usually the case when blood flow is not severely compromised, the tourniquet pressure and acceptable ischemia time must be discussed with the surgeon beforehand and carefully followed. With noncritical cases of vascular insufficiency, a simple preoperative test of noting the reperfusion time following a brief period of ischemia can be used as a guide for acceptability of the tourniquet.

Couse NF, Delaney CP, Horgan PG, et al. Pulse oximetry in the diagnosis of non-critical peripheral vascular insufficiency. *J R Soc Med.* 1994;87:511–512.

Hines RL, Greene NM, eds. *Stoelting's Anesthesia and Co-existing Disease.* 5th ed. Philadelphia: Saunders; 2008:516–517.

C.2. Which peripheral nerve blocks can be used for exploration of the metatarsals? What are the landmarks for an ankle block?

For complete anesthesia of the foot, each of the five nerves to the foot must be individually blocked. With the exception of the saphenous nerve (which is the extension of the femoral nerve), all of the nerves are derived from the sciatic nerve. Various techniques and landmarks have been described by numerous authors, but essentially, the two major nerves supplying motor function to the foot, the posterior tibial, and the deep peroneal require individual needle insertion, whereas the sensory nerves to the foot (superficial peroneal, saphenous, and sural) can be blocked by a common subcutaneous ring.

To approach the posterior tibial nerve, the foot is dorsiflexed to 90 degrees. The patient is placed either prone with the leg straight or supine with the operated leg flexed and supported by the opposite leg. A fine gauge needle (25G to 27G) is inserted along the medial border of the Achilles tendon at the level of the medial malleolus and advanced to contact the posterior tibia. One must be aware that the posterior tibial artery often lies between the nerve and the tibial periosteum. The local anesthetic solution (without epinephrine) 3 to 5 mL is injected if paresthesia is encountered during needle insertion; otherwise, 5 to 7 mL is injected just superficial to the periosteum (Fig. 46.1).

The deep peroneal nerve at the ankle lies deep between the tendons of the tibialis anterior and the extensor hallucis longus (EHL). These tendons are identified by asking the patient to dorsiflex the big toe (EHL) and the ankle (tibialis anterior). Traditionally, the nerve is blocked here (Fig. 46.2). Because this nerve courses behind

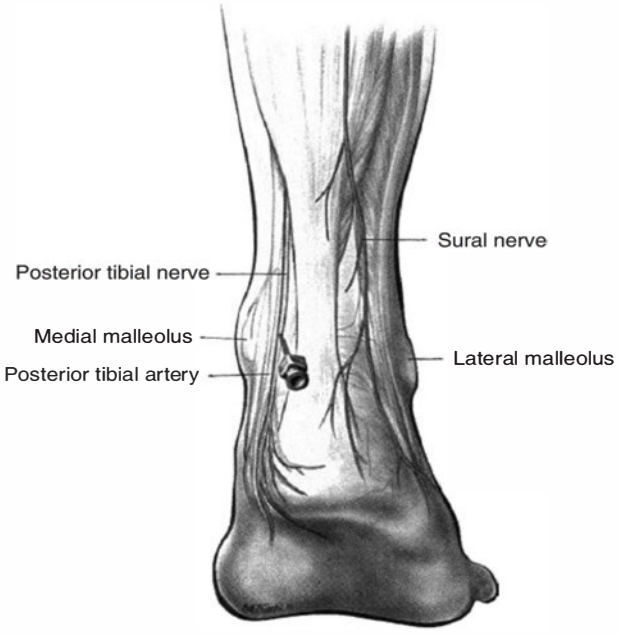


Figure 46.1 The posterior tibial nerve block.

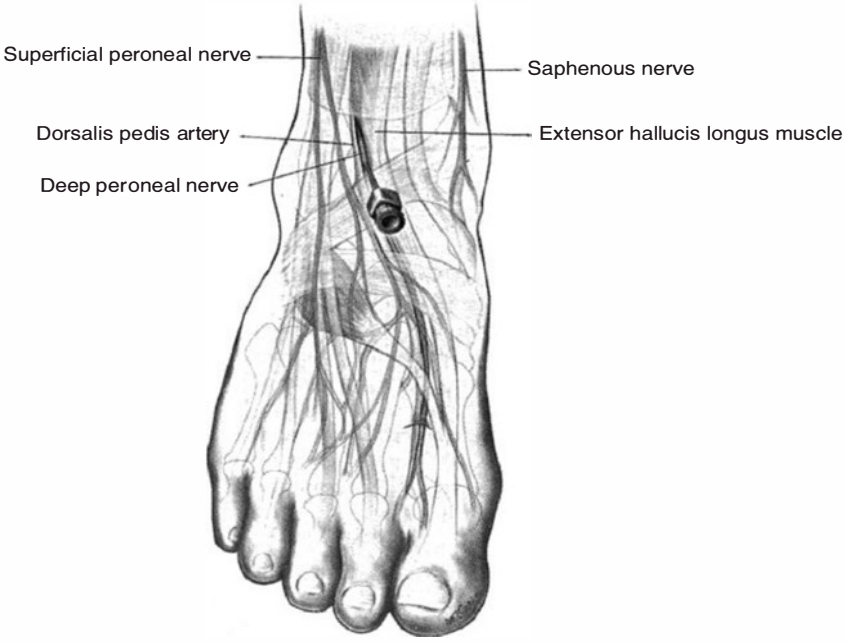


Figure 46.2 The deep peroneal nerve block.

the EHL to emerge just lateral to the EHL tendon on the dorsum of the foot in proximity to the anterior tibial artery, it can be more easily blocked by using the "midtarsal" approach as described by Sharrock et al. (Fig. 46.3, needle B). With this method, the dorsalis pedis pulsation is first located lateral to the EHL tendon at the midfoot, just distal to the extensor retinaculum. A fine-gauge needle is inserted immediately lateral to the arterial pulse until contact is made with periosteum. After withdrawing the needle 2 to 3 mm off the periosteum, 2 to 3 mL of the local anesthetic solution (without epinephrine) should be injected.

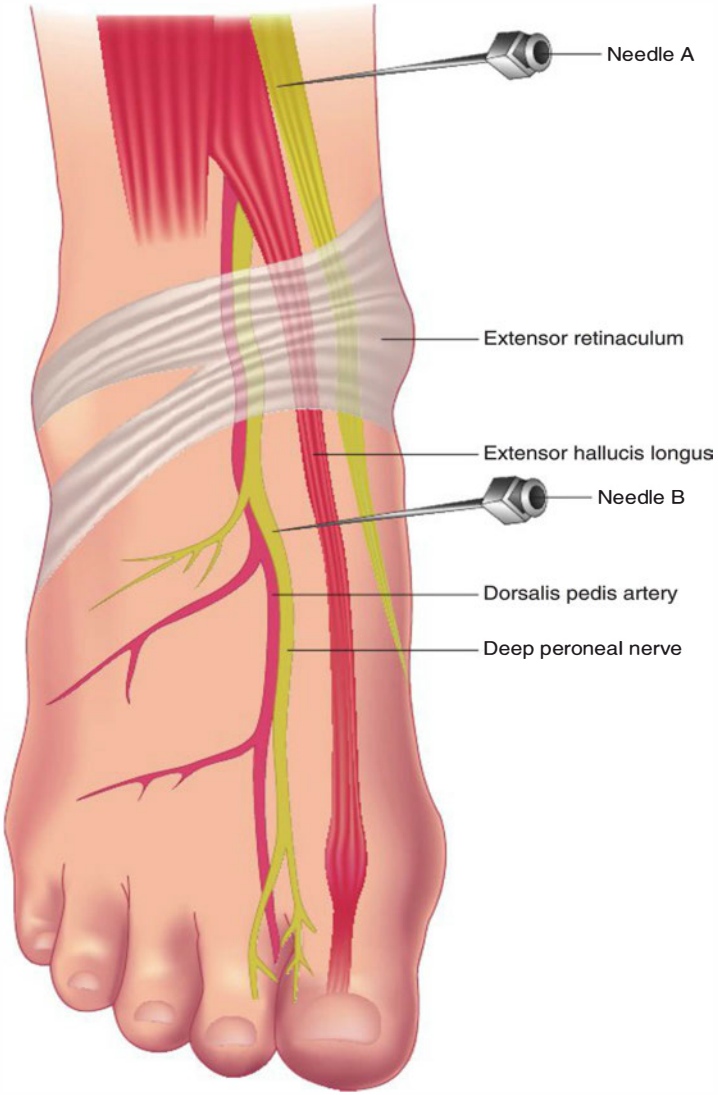


Figure 46.3 Ankle block, Sharrock's midtarsal approach.

From the same needle puncture site as the deep peroneal nerve block, the needle can be redirected to block the branches of the superficial peroneal, saphenous, and sural nerves by making a subcutaneous ring across the dorsum of the foot using 3 to 5 mL of the anesthetic solution (without epinephrine). An alternative to blocking the sural nerve (which is necessary in this patient but may not be necessary for surgery on the great toe, for example), the patient is positioned as for the posterior tibial nerve block, and the needle is inserted immediately lateral to the Achilles tendon at the level of the lateral malleolus in an anterolateral direction. The needle is advanced until contact is made with bone or paresthesia is elicited, and 3 to 5 mL of the local anesthetic is injected.

Benzon HT, Rathmell JP, Wu CL, et al., eds. *Raj's Practical Management of Pain*. 4th ed. St. Louis: Mosby Elsevier; 2008:897–898.

Brown DL. *Atlas of Regional Anesthesia*. 3rd ed. Philadelphia: Saunders; 2006:139–143.

Meier G, Buettner J, eds. *Peripheral Regional Anesthesia: An Atlas of Anatomy and Techniques*. 2nd ed. Stuttgart: Thieme; 2007:203–213.

Sharrock NE, Waller JF, Fierro LE. Midtarsal block for surgery of the forefoot. *Br J Anaesth*. 1986;58:37–40.

C.3. What are the advantages and disadvantages of an ankle block?

The main advantages of an ankle block lie in its relative simplicity and safety. The landmarks used in performing this block are readily identified in the majority of patients, and precise localization of each nerve is not necessary with this "field block" technique. Major hemodynamic changes associated with neuraxial techniques are avoided. The main complication of the ankle block is direct intraneural injection of the local anesthetic solution. Short of direct intravascular injections, systemic toxic effect from the usual volume (15 to 20 mL) of local anesthetic agents is unlikely because of slower uptake and distribution of the local anesthetic into the central compartment.

The two main disadvantages of this block are the discomfort associated with the performance of the block and the inability to use a pneumatic tourniquet, unless it is placed just supramalleolarly around the well-padded ankle. The ankle block is uncomfortable for most patients because of the multiple needle insertions involved, as well as the abundance of nerve endings in the foot and ankle region, which makes it extremely sensitive to needle injections. Adequate sedation is recommended before carrying out the block. In addition, the long tendons of the foot continue to work because the muscles have their nerve supply more proximally and the patient must be reminded not to move the foot during surgery.

When prolonged numbness can be tolerated by the patient and is acceptable to the surgeon, the patient can be relieved of postsurgical pain for many hours with long-acting local anesthetic agents such as bupivacaine. Both the patient and the surgical team must be forewarned of the anticipated delay in sensory and motor recovery to allay anxiety during the immediate postoperative period.

Benzon HT, Rathmell JP, Wu CL, et al., eds. *Raj's Practical Management of Pain*. 4th ed. St. Louis: Mosby Elsevier; 2008:897–898.

Hadzic A, Vloka J. Peripheral nerve blocks: principles and practice. *New York School of Regional Anesthesia*. Available at: http://www.nysora.com/techniques/ankle_block/

Lichtenfeld NS. The pneumatic ankle tourniquet with ankle block anesthesia for foot surgery. *Foot Ankle*. 1992;13:344–349.

Mineo R, Sharrock NE. Venous levels of lidocaine and bupivacaine after midtarsal ankle block. *Reg Anesth*. 1992;17:47–49.

C.4. What other peripheral regional anesthetic techniques may be appropriate?

Several other methods may be used to provide regional anesthesia for this patient. Although less common today than other more frequently used and safer techniques, it is possible to use an intravenous regional block when venous access is available. For tourniquets placed on the calf, 30 mL of a 0.5% lidocaine solution injected after exsanguination usually suffices. If the tourniquet is placed on the thigh, 50 to 60 mL will be needed. The downside of this technique is that the exsanguination process may be painful related to tourniquet pain or those patients with a fracture. In addition, accidental loosening of the tourniquet too quickly could result in significant systemic toxicities and complications.

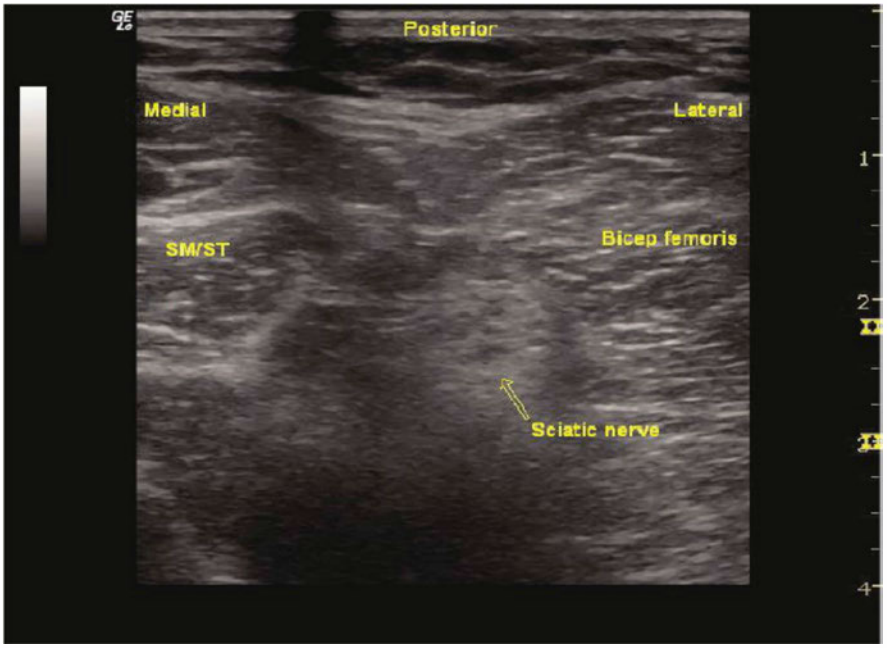
Alternatively, the sciatic nerve (consisting of the tibial and common peroneal nerves) (Fig. 46.4) and saphenous nerve can be blocked separately above the level of the knee joint. At this level, the exact location of the saphenous nerve is variable but it is usually within Hunter canal (Fig. 46.5). If ultrasound imaging is used, the sciatic nerve can be consistently found at the top center of the popliteal fossa just lateral to the popliteal pulse, before its division into the tibial and common peroneal nerves (popliteal block). The sciatic nerve can be blocked at this level with the patient in the prone, lateral, or supine position (with the leg flexed at the hip and the knee).

The classic intertendinous technique involves the identification of the popliteal triangle, which is defined by the tendon of the biceps femoris laterally, the tendons of the semitendinosus and semimembranosus medially, and the popliteal fossa crease. The point of needle insertion varies among different authors, but generally, the nerve can be identified 7 cm above the popliteal crease, at the midpoint between the tendons, or 9 cm above the popliteal crease, 1 cm lateral to the midline of the triangle (Fig. 46.6). Localization of the nerve can be achieved using a paresthesia-seeking technique, a nerve stimulation technique, if ultrasound imaging is not available. Using a nerve stimulation technique, plantar flexion and inversion of the foot (ideally), or dorsiflexion and eversion of the foot, is sought with 0.2- to 0.5-mA current.

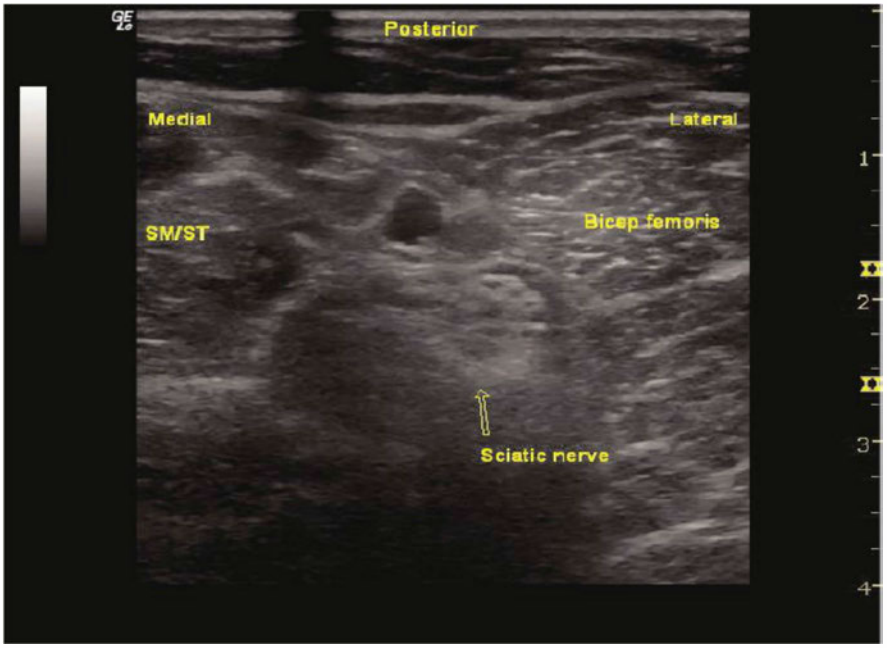
Using anesthetic solutions in higher concentrations (such as 2% lidocaine with bicarbonate or 0.75% bupivacaine) with these nerve blocks, the motor nerves to the long tendons of the ankle, as well as the sensory supply to the lower leg and foot, are anesthetized. Patient movement during foot surgery is thus minimized. A major benefit of popliteal over ankle block is that it allows the use of a calf tourniquet. In addition, popliteal catheters are becoming increasingly popular in clinical practice for postoperative pain management.

Combined femoral and sciatic nerve blocks with adequate sedation may provide an alternative to neuraxial techniques for achieving anesthesia below the knee. Although the obturator nerve also innervates the knee, its sensory terminals supply only a small area of skin just medial and superior to the knee joint. The area involved can easily be anesthetized, if necessary, with local infiltration by the surgeon. In this patient, the surgery is in the foot; a femoral and sciatic combination would provide adequate surgical analgesia.

The femoral nerve provides sensory innervation to most of the anterior knee and can be blocked in the supine patient by injection at the femoral triangle (Fig. 46.7). The needle insertion site is immediately lateral to the femoral pulse at the level of the inguinal ligament (classical landmark) or at the level of the femoral crease. The further one moves from the inguinal canal, the more likely the nerve has divided into posterior and anterior divisions. If using a nerve stimulator, a patellar twitch (stimulation of quadriceps contraction) at 0.2- to 0.5-mA current is sought. Otherwise, the nerve can be localized by seeking paresthesia consistent with the distribution of the nerve or by ultrasound guidance (Fig. 46.8). Injection of 0.5% bupivacaine 10 to 25 mL here will usually provide adequate surgical anesthesia. It is also possible to place an indwelling catheter for postoperative infusion. In this patient, because the metatarsal



A



B

Figure 46.4 **A.** Popliteal block before injection. **B.** Popliteal block after injection. SM/ST: semimembranosus/semitendinosus. (Courtesy Hospital for Special Surgery.)

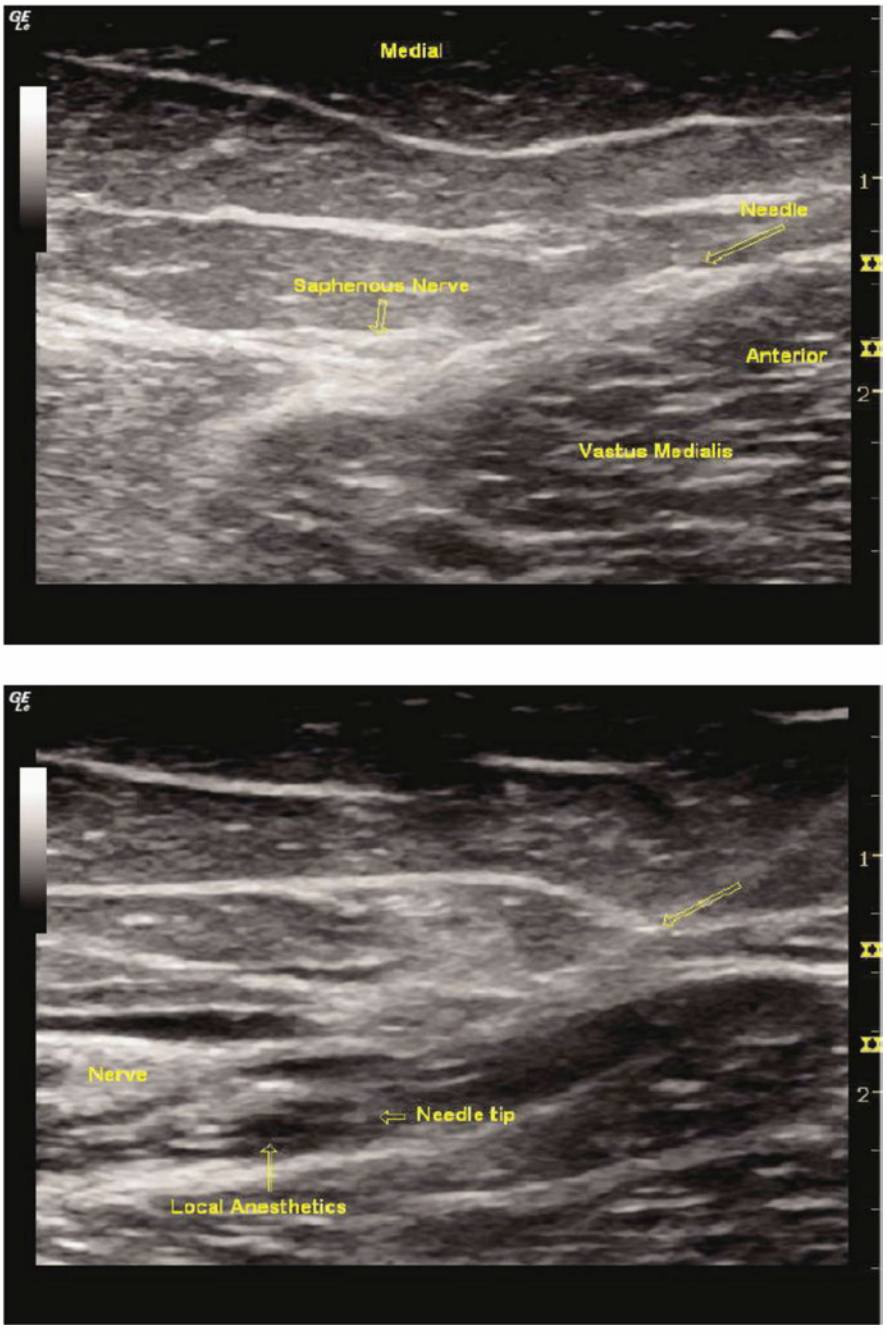


Figure 46.5 **A.** Saphenous block before injection. **B.** Saphenous block after injection. (Courtesy Hospital for Special Surgery.)

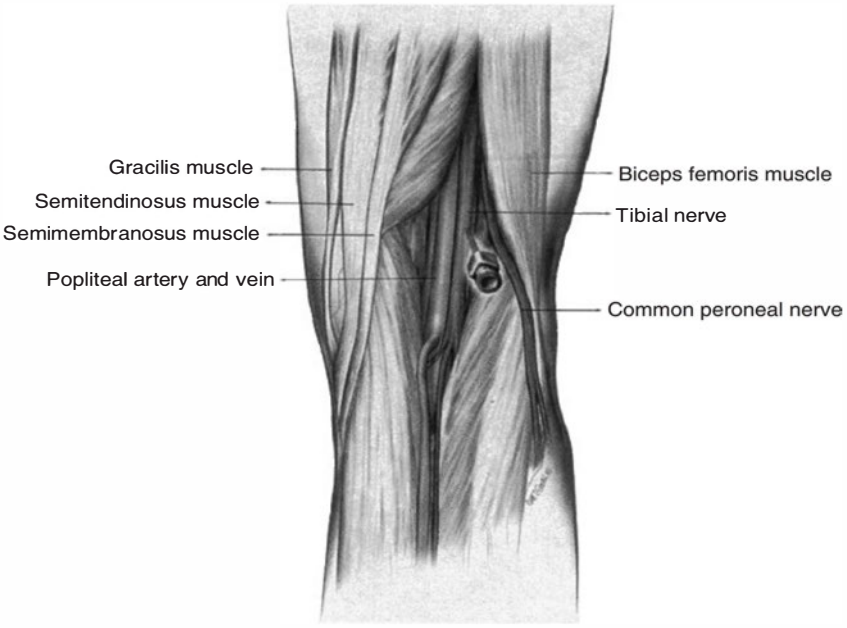


Figure 46.6 Classic posterior approach of tibial nerve block.

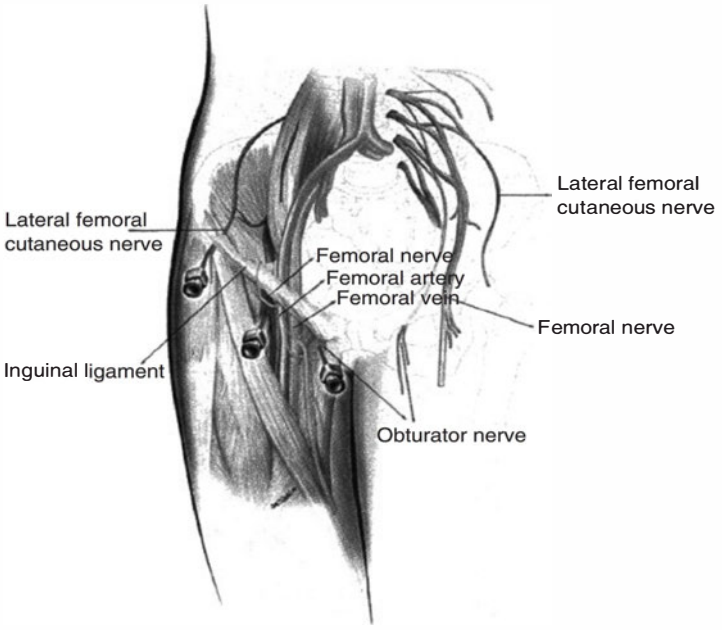


Figure 46.7 The femoral nerve block, lateral femoral cutaneous nerve block, and obturator nerve block.

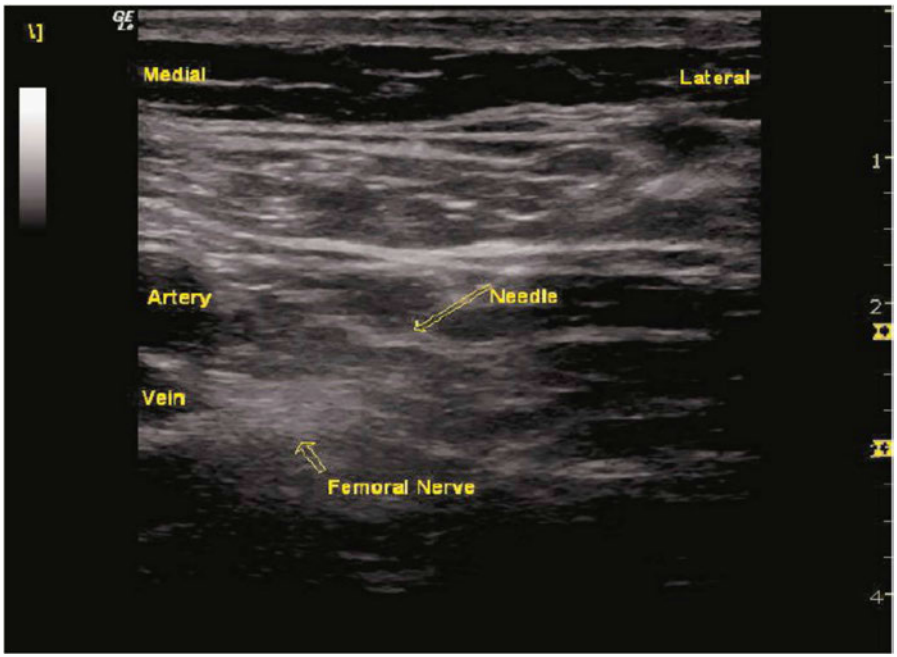


Figure 46.8 Femoral nerve block. (Courtesy Hospital for Special Surgery.)

damage is lateral, the surgical pain would be less in the femoral distribution and more likely in the sciatic distribution, which may lessen the efficacy of a femoral catheter.

A variation of the femoral nerve block is the fascia iliaca block (Fig. 46.9), which was first described by Dalens. This technique does not require a nerve stimulator or the seeking of paresthesia. A line is drawn between the anterior superior iliac spine and the pubic tubercle and divided into thirds. The needle insertion point is made 1 cm caudad to this line, two-thirds of the distance from the pubic tubercle. Two "pops" may be felt as the needle pierces the fascia lata and then the fascia iliaca. The use of a short bevel or pencil-tipped needle may enhance the appreciation of the "pops." The local anesthetic solution (20 to 25 mL) is then injected. Both the fascia iliaca and femoral nerve blocks are effective in providing postoperative analgesia, but the fascia iliaca block is more likely to block the lateral femoral cutaneous nerve as well.

The sciatic nerve can be blocked using several different approaches. The posterior approach (classically described by Labat, with modified approaches described by Winnie, Raj, DiBenedetto, and others) requires placement of the patient with the operative side up and the hip and knee flexed (Sim's position). A description of all the posterior approaches to the sciatic nerve is beyond the scope of this chapter. In essence, these modified approaches use anatomic landmarks that are easier to locate in patients than with the Labat technique and they block the sciatic nerve more distally in the leg, thus avoiding painful needle insertion through the gluteal muscles.

The landmarks for the classical approach by Labat are determined by first drawing a line from the greater trochanter to the posterior superior iliac spine (Fig. 46.10). Winnie modified this approach by adding a second line, drawn from the greater trochanter to the sacral hiatus. From the midpoint of the posterior superior iliac spine line, another line is drawn perpendicularly to meet the sacral hiatus line.

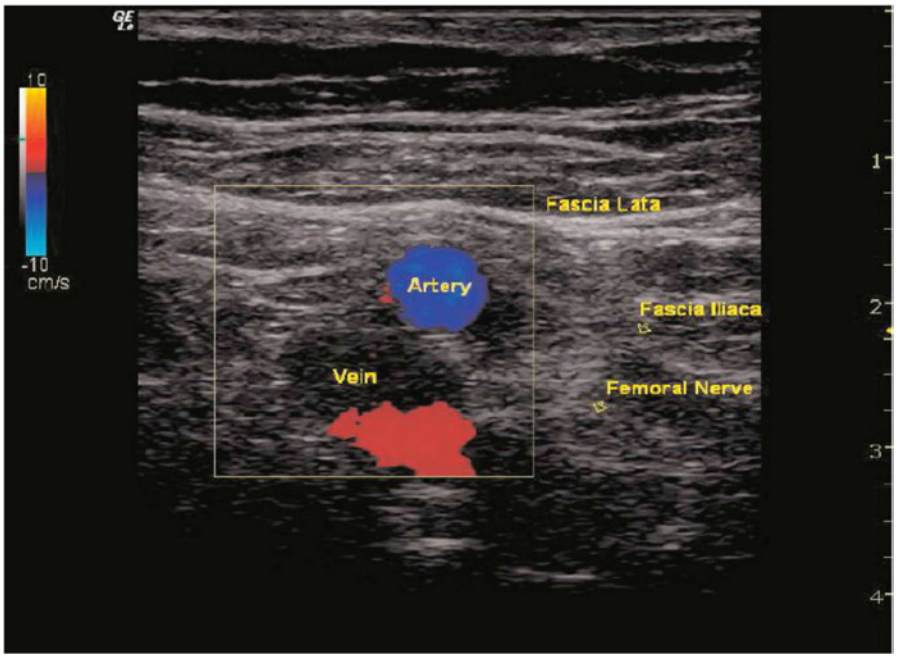


Figure 46.9 Fascia iliaca block. (Courtesy Hospital for Special Surgery.)

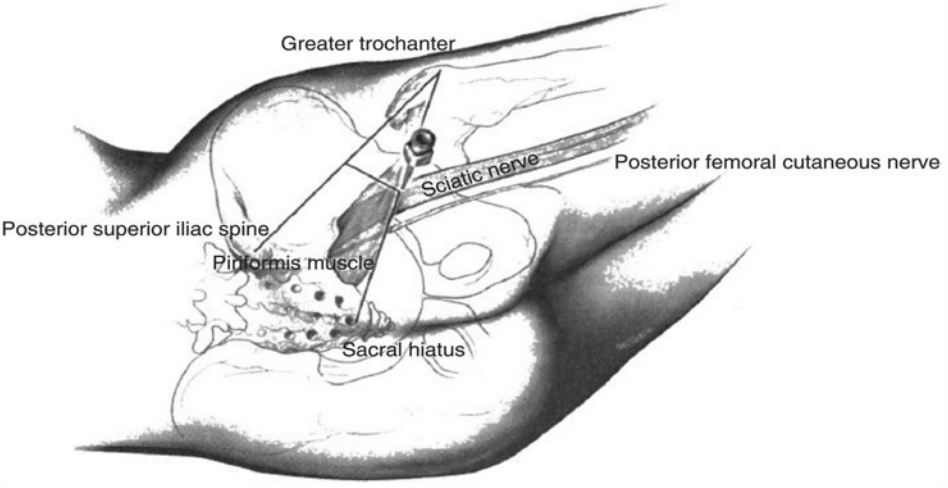


Figure 46.10 Sciatic nerve block; the Labat approach.

The intersection of the perpendicular line and the sacral hiatus line is the needle insertion point. As with the popliteal block (which in essence is a distal sciatic nerve block; see earlier discussion), localization of the nerve can be achieved using a paresthesia-seeking technique or a nerve stimulation technique. Ideally, the paresthesia should be below the knee. Using a nerve stimulation technique, plantar flexion and inversion of the foot (ideally) or dorsiflexion and eversion of the foot are sought at 0.2- to 0.5-mA current. A volume of 20 to 25 mL of the anesthetic solution will be needed to cover the nerve adequately.

If the patient cannot be turned lateral, an anterior approach to the sciatic nerve may be employed. In the supine patient, a line is drawn along the inguinal ligament from the anterior superior iliac spine to the pubic tubercle and is trisected. Another line is drawn from the tip of the greater trochanter inferomedially parallel to the inguinal line. At the junction of the medial and second third of the trisected line, a perpendicular line is drawn to meet the trochanteric line. The intersection is the point of needle entry. A needle inserted here vertically will contact the medial border of the femur at the lesser trochanter. The needle is then directed slightly medially to pass the medial femoral surface. Either muscle stimulation (as described above) or paresthesia should be sought about 5 cm deep to the femur. The posterior femoral cutaneous nerve, which leaves the main trunk early, may be missed by this approach.

Benzon HT, Rathmell JP, Wu CL, et al., eds. *Raj's Practical Management of Pain*. 4th ed. St. Louis: Mosby Elsevier; 2008:893–897.

Dalens B, Vanneuville G, Tanguy A. Comparison of the fascia iliaca compartment with "3-in-1" block in children. *Anesth Analg*. 1989;69:705–713.

Enneking FK, Chan V, Greger J, et al. Lower-extremity peripheral nerve blockade: essentials of our current understanding. *Reg Anesth Pain Med*. 2005;30:4–35.

Meier G, Buettner J, eds. *Peripheral Regional Anesthesia: An Atlas of Anatomy and Techniques*. 2nd ed. Stuttgart: Thieme; 2007:111–122, 126–156, 159–160.

Rogers JN, Ramamurthy S. Lower extremity blocks. In Brown DL, ed. *Regional Anesthesia and Analgesia*. Philadelphia: WB Saunders; 1996: 279–291

Shah S, Tsai T, Iwata T, et al. Outpatient regional anesthesia for foot and ankle surgery. *Int Anesthesiol Clin*. 2005;43:143–151.

C.5. How is ultrasound guidance useful in performing peripheral nerve blocks?

Most peripheral nerve blocks rely on surface anatomic landmarks (bone, vascular, muscular, grooves) to guide initial needle placement. Nevertheless, many studies have demonstrated the unreliability of these landmarks because of wide interpatient variability in nerve location relative to the surface landmarks. Also, in patients with peripheral vascular disease, absent or faint pulse is a poor landmark.

Anatomic landmarks only guide the initial needle placement and ultrasound probe position. Techniques such as electrical nerve stimulation or seeking of paresthesia have been used to more precisely localize the nerve, but neither of these techniques can rule out an intraneural injection. In addition, once the local anesthetic injection has begun, it is impossible to know whether the needle tip position has changed unless there is a form of direct visualization. Ultrasound imaging offers several advantages. First, it provides direct visualization of nerves, which allows selection of the best needle insertion site. Second, it provides real-time guidance for the needle advancing toward the target nerve, thus minimizing "hunting" for the nerve and potential complications such as vascular injury. Finally, direct observation of local anesthetic spread at the time of injection helps the operator to ensure the local anesthetic is deposited completely around the nerves.

Studies by Marhofer and Williams have shown shorter onset time, improved block quality, and reduced arterial puncture (Marhofter's study only) during the performance of femoral blocks and supraclavicular blocks. Despite the purported benefits, there are still proponents of anatomic methods. In our scenario, an ultrasound-guided block may be less critical for conducting the ankle block because surface landmarks are easily identifiable there. In any other nerve block, more proximal within the lower extremity, including femoral nerve, sciatic nerve, saphenous nerve, or popliteal block, ultrasound guidance would offer greater assistance.

Awad IT, Chan V. Ultrasound imaging of peripheral nerves: a need for a new trend. *Reg Anesth Pain Med.* 2005;30:321–323.

Bigeleisen PE, Orebaugh SL, Moayeri N, et al., eds. *Ultrasound-guided Regional Anesthesia and Pain Medicine*. Philadelphia: Lippincott Williams & Wilkins; 2010:97–103, 108–113, 132–139, 140–143.

Harmon D, Frizelle HP, Sandhu NS, et al., eds. *Perioperative Diagnostic and Interventional Ultrasound*. Philadelphia: Sauders Elsevier; 2008:153–158, 164–173.

Marhofer P, Schrogendorfer K, Koining H, et al. Ultrasonographic guidance improves sensory block and onset time of three-in-one blocks. *Anesth Analg.* 1997;85:854–857.

Williams SR, Chouinard P, Arcand G, et al. Ultrasound guidance speeds the execution and improves the quality of supraclavicular block. *Anesth Analg.* 2003;97:1518–1523.

C.6. What are the risks of peripheral nerve block in an immune-compromised patient?

Three case reports so far have been written about serious infectious complications of peripheral nerve blocks; two of the three cases occurred in immunocompromised patients, but no recommendations have been developed because data are still sparse to date.

Horlocker TT, Wedel DJ. Regional anesthesia in the immunocompromised patient. *Reg Anesth Pain Med.* 2006;31:334–345.

D. Postoperative Management

D.1. How should the postoperative pain be managed in this patient?

A multimodality approach to postoperative pain management may include nonsteroidal anti-inflammatory drugs, acetaminophen, opioids, anticonvulsants, regional anesthesia, and ketamine. Intraoperative ketorolac or preoperative administration of a COX-2 inhibitor may be useful in reducing opioid requirements. Opioids, whether given via patient-controlled systems or by nurses, should be given before sensations fully recover from the regional anesthetic and pain becomes severe. Specifically in patients with chronic pain, such as this patient, it is important to treat both the chronic baseline of pain as well as the new onset acute surgical pain. Chronic cancer pain, in addition, will have episodes of peaks and troughs outside of the typical pain expected after a procedure and must be addressed with specific care.

Although this patient may have undergone only a comparatively minor foot surgery, he nonetheless has a history of altered regulation of his receptors because of chronic cancer pain. For this reason, options for prolonged postoperative pain control may include intraoperative injection of local anesthetic, morphine, clonidine,

or ketorolac by the surgeon. One can also consider continuous nerve blocks for postoperative analgesia with local anesthetic infusion via an indwelling catheter.

Brill S, Plaza M. Non-narcotic adjuvants may improve the duration and quality of analgesia after knee arthroscopy: a brief review. *Can J Anesth.* 2004;51:975–978.

Farrer JT, Young JP Jr, LaMoreaux L, et al. Clinical importance of changes in chronic pain intensity measured on an 11-point numerical pain rating scale. *Pain.* 2001;94:149–158.

Macario A, Lipman A. Ketorolac in the era of cyclo-oxygenase-2 selective nonsteroidal anti-inflammatory drugs: a systematic review of efficacy, side effects, and regulatory issues. *Pain Med.* 2001;2:336–351.

Straube S, Derry S, McQuay HJ, et al. Effect of preoperative Cox-II-selective NSAIDs (coxibs) on postoperative outcomes: a systematic review of randomized studies. *Acta Anaesthesiol Scand.* 2005;49:601–613.

World Health Organization. *Cancer Pain Relief and Palliative Care: Report of WHO Expert Committee.* 3rd ed. Geneva, Switzerland: WHO; 1996.

D.2. Why should the neurovascular status of the foot be followed?

It is important to follow the neurovascular function of the lower extremity for a period of 24 to 36 hours because there is a relatively higher incidence of persistent paresthesia following foot and ankle surgery. This may be a result of the nerve blocks or tight surgical dressings. During this period, the patient should be encouraged to report any abnormal sensations and the surgical dressing should be carefully examined to ensure that there is no circulatory compromise or nerve compression. In the longer term, the patient should be followed for possible neuroma formation both at the needle insertion and the surgical sites. The natural history of any pre-existing neurologic dysfunction should be considered when evaluating any reported complications.

Benzon HT, Rathmell JP, Wu CL, et al., eds. *Raj's Practical Management of Pain.* 4th ed. St. Louis: Mosby Elsevier; 2008:899–900.

Kofoed H. Peripheral nerve blocks at the knee and ankle in operations for common foot disorders. *Clin Orthop.* 1982;168:97–101.

E. Summary

Although the surgery may be localized to a distal extremity, the anesthetic requirement may be much more extensive. This is especially crucial in patients who have comorbidities that can affect immune status and coagulation. The preoperative evaluation of the patient must be as comprehensive as with any other operations. The anesthetic techniques outlined in this chapter offer flexibility to cover most demands of the surgery, yet ensure the least physiologic disturbance in a safe and conservative manner.

CHAPTER 47

Complex Regional Pain Syndromes

Sudhir A. Diwan, Vinod Malhotra, and Neel D. Mehta

A 35-YEAR-OLD WOMAN complains of diffuse burning pain in the left arm and hand for the last 6 months. She recalls spraining her left wrist while playing volleyball. Her left hand feels colder than the right, and her fingertips are blue. She is a recently divorced high-profile executive.

A. Medical Disease and Differential Diagnosis

1. What is the differential diagnosis of pain in this patient?
2. What is complex regional pain syndrome (CRPS)?
3. What are the two types of CRPS?
4. What are the diagnostic criteria for CRPS? What is the incidence of this disease?
5. Define allodynia, hyperalgesia, hyperesthesia, and dysesthesia.
6. What are the associated stages of CRPS?
7. What are the possible etiologies of CRPS?
8. Explain the pathophysiology of the development of CRPS.
9. Define sympathetically maintained pain (SMP) and sympathetically independent pain (SIP).
10. How does CRPS differ from neuralgia?
11. What is central pain? How will you differentiate central pain from CRPS?
12. Is the social history of this patient relevant to the development of chronic pain?

B. Pain Management

1. How will you work up CRPS types I and II?
2. Describe the sympathetic nerve supply to the arm.
3. Where is the stellate ganglion located?
4. What are the anatomic landmarks used in the stellate ganglion block?
5. What are the clinical signs of stellate ganglion block?
6. What is Horner syndrome?

7. After a stellate ganglion block, this patient reports no significant change in the degree of pain despite evidence of Horner syndrome. Is the pain psychogenic in this patient?
8. What types of nerve fibers are interrupted in stellate ganglion block?
9. What is a differential block?
10. What are the two major classes of local anesthetics? Describe the major differences in their clinical pharmacology.
11. What factors determine the onset, potency, and duration of a local anesthetic block?
12. How does the addition of epinephrine to commercially available premixed solutions affect the efficacy of local anesthetics?
13. How will you treat this patient?
14. What is the pharmacologic management of CRPS?
15. What is the role of intravenous regional block (Bier method) in diagnosis and treatment of CRPS?
16. Compare and contrast the mechanism of action of ketamine and methadone.
17. What role does ketamine infusion play in the treatment of CRPS?
18. What is the role of spinal cord stimulation (SCS) and surgical sympathectomy?

C. Complications

1. What are the complications of stellate ganglion block?
2. What is the systemic toxicity of local anesthetics?
3. How do you treat the systemic toxicity of local anesthetic drugs?

A. Medical Disease and Differential Diagnosis

A.1. What is the differential diagnosis of pain in this patient?

Pain accompanied by burning and temperature change in this patient is most likely due to CRPS. The differential diagnosis may also include the following:

1. Peripheral neuropathy
2. Soft tissue injury
3. Vascular insufficiency (Raynaud disease)
4. Nerve entrapment syndrome (carpal tunnel syndrome)
5. Brachial plexopathy

Over the years, CRPS has been referred to as *reflex sympathetic dystrophy* (RSD), causalgia, sympathetically maintained pain (SMP), and chronic peripheral pain syndrome. The term CRPS was introduced in 1994 by the International Association for the Study of Pain subcommittee on taxonomy. It is subdivided into CRPS type I (formerly described as RSD) and CRPS type II (formerly described as causalgia).

Ballantyne JC, Rathmell JP, Fishman SM, eds. *Bonica's the Management of Pain*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:314–331.

Boas RA. Complex regional pain syndromes: symptoms, signs, and differential diagnosis. In: Janig W, Stanton Hicks M, eds. *Reflex Sympathetic Dystrophy: A Reappraisal. Progress in Pain Research and Management*. Seattle: IASP Press; 1996:79–92.

Merskey H, Bogduk N. Classification of chronic pain. In: Task Force on Taxonomy. International Association for the Study of Pain. *Relatively Generalized Syndromes*. 2nd ed. Seattle: IASP Press; 1994:39–56.

Stanton-Hicks M, Janis W, Hassenburch S. Reflex sympathetic dystrophy: changing concepts and taxonomy. *Pain*. 1995;63:127–133.

A.2. What is complex regional pain syndrome (CRPS)?

CRPS is characterized by pain with sudomotor or vasomotor instability. CRPS is triggered by *noxious stimuli* (type I) or by *nerve injury* (type II). It is not limited to the distribution of a single peripheral nerve and is disproportionate to the inciting event.

RSD, causalgia, algodystrophy, Sudeck atrophy, and various other conditions are all grouped under CRPS. This diagnosis is better descriptive of the wide range of clinical signs and symptoms and the complexity of the pathophysiology responsible for the clinical picture.

Ballantyne JC, Rathmell JP, Fishman SM, eds. *Bonica's the Management of Pain*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:314–331.

Merskey H, Bogduk N. Classification of chronic pain. In: Task Force on Taxonomy. International Association for the Study of Pain. *Relatively Generalized Syndromes*. 2nd ed. Seattle: IASP Press; 1994:39–56.

Stanton-Hicks M, Janis W, Hassenburch S. Reflex sympathetic dystrophy: changing concepts and taxonomy. *Pain*. 1995;63:127–133.

A.3. What are the two types of CRPS?

CRPS-I is defined as a clinical syndrome triggered by a *noxious stimulus* that is not limited to the distribution of a single peripheral nerve. CRPS-II is defined as a clinical syndrome that is due to a *nerve injury* and is mostly limited to the distribution of the injured nerve. The diagnostic criteria are the same for CRPS-I and II.

Ballantyne JC, Rathmell JP, Fishman SM, eds. *Bonica's the Management of Pain*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:314–331.

Boas RA. Complex regional pain syndromes: symptoms, signs, and differential diagnosis. *Clin J Pain*. 1998;14:48–54.

Janig W, Stanton Hicks M, eds. *Reflex Sympathetic Dystrophy: A Reappraisal. Progress in Pain Research and Management*. Seattle: IASP Press; 1996:79–92.

Stanton-Hicks MD, Burton AW, Bruehl SP, et al. An updated Interdisciplinary clinical pathway for CRPS: report of an expert panel. *Pain Pract*. 2000;2:1–16.

Veldman PH, Reynen HM, Arntz IE, et al. Signs and symptoms of reflex dystrophy: prospective study of 829 patients. *Lancet*. 1993;342:1012–1016.

A.4. What are the diagnostic criteria for CRPS? What is the incidence of this disease?

The diagnosis of CRPS can be made in the following context: A history of trauma to the affected area associated with pain that is disproportionate to the inciting event plus one or more of the following:

- Abnormal function of the sympathetic nervous system
- Swelling
- Movement disorder
- Changes in tissue growth (dystrophy and atrophy)

The main features include pain that is continuous, burning in nature, independent of type and severity of injury, and not limited to a dermatomal distribution. Patients may complain of allodynia, dysesthesia, or hyperalgesia. Movement and stress exacerbate pain. Edema is usually present. Abnormal sudomotor activity, limb discoloration, and local temperature changes are common but inconsistent.

It affects between 200,000 and 1.2 million Americans. This syndrome may follow as many as 5% of all traumatic injuries.

Ballantyne JC, Rathmell JP, Fishman SM, eds. *Bonica's the Management of Pain*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:314–331.

Merskey H, Bogduk N. Classification of chronic pain. In: Task Force on Taxonomy. International Association for the Study of Pain. *Relatively Generalized Syndromes*. 2nd ed. Seattle: IASP Press; 1994:39–56.

A.5. Define allodynia, hyperalgesia, hyperesthesia, and dysesthesia.

- *Allodynia*. Pain caused by a stimulus that normally does not provoke pain (i.e., touching with a cotton swab).
- *Hyperalgesia*. An increased response to a stimulus that is normally painful (i.e., increased response to pinprick).
- *Hyperesthesia*. Increased sensitivity to a stimulus either due to a diminished threshold or an increased response to stimuli that are normally recognized. Hyperesthesia includes both allodynia and hyperalgesia.
- *Dysesthesia*. An abnormal sensation that is unpleasant to the patient. It may be either spontaneous or evoked (i.e., lumbar radiculopathy).

Ballantyne JC, Rathmell JP, Fishman SM, eds. *Bonica's the Management of Pain*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:314–331.

A.6. What are the associated stages of CRPS?

Stage I

- Onset of severe pain limited to the site of injury
- Increased sensitivity of skin to touch and light pressure (hyperesthesia)
- Localized swelling
- Muscle cramps
- Stiffness and limited mobility

At onset, skin is usually warm, red, and dry; then it may change to blue (cyanotic) in appearance and become cold and sweaty.

- Increased sweating (hyperhydrosis)
- In mild cases, this stage lasts a few weeks and then subsides spontaneously or responds rapidly to treatment.

Stage II

- Pain becomes even more severe and more diffuse.
- Swelling tends to spread and may change from a soft to hard (brawny) type.
- Hair may become coarse then scant, nails may grow faster and become brittle, cracked, and heavily grooved.
- Spotty wasting of bone (osteoporosis) occurs early but may become severe and diffuse.
- Muscle wasting begins.

Stage III

- Marked wasting of tissue (atrophic) eventually becomes irreversible.
- For many patients, the pain becomes intractable and may involve the entire limb.
- A small percentage of patients have developed generalized *reflex sympathetic dystrophy* (RSD), affecting the entire body.

Ballantyne JC, Rathmell JP, Fishman SM, eds. *Bonica's the Management of Pain*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:314–331.

A.7. What are the possible etiologies of CRPS?

CRPS may follow relatively minor trauma with or without nerve injury. Causes leading to CRPS include the following:

- Injuries to peripheral tissues (e.g., fractures, dislocations, and postoperative state)
- Inflammatory conditions (e.g., fasciitis, tendonitis, bursitis, and arthritis)
- Immobilization as a result of injury or cast application
- Peripheral nerve injury resulting from direct compression or ischemia (e.g., brachial plexopathy, postherpetic neuralgia, and nerve root injury)
- Central nervous system insults (e.g., head injury, ischemia, and brain tumor)
- Spinal cord lesions
- Idiopathic

Ballantyne JC, Rathmell JP, Fishman SM, eds. *Bonica's the Management of Pain*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:314–331.

Veldman PH, Reynen HM, Arntz IE, et al. Signs and symptoms of reflex dystrophy: prospective study of 829 patients. *Lancet*. 1993;342:1012–1016.

A.8. Explain the pathophysiology of the development of CRPS.

Several hypotheses have been postulated but none can explain all of the findings and the varying responses to treatment in these patients. These hypotheses include the following:

- Abnormal discharges in sympathetic and nociceptive afferents produced by trauma
- Sensitization of peripheral sensory receptors produced by sympathetic hyperactivity
- Formation of ephapses (artificial synapses) after peripheral nerve injury
- Spontaneous neuronal ectopy at the site of demyelination or axonal injury
- Central reorganization of pain processing (central sensitization)

More than one sequence of events likely take place in a patient, giving rise to a mixed clinical picture. A dynamic change in the physiology and structure of central pain projecting neurons mediated through the N-methyl-D-aspartic acid (NMDA) receptor. Injury initiates and maintains a state of central sensitization in the central pain pathways, resulting in a lower threshold to fire pain transmission neurons and increases their receptive fields. This often leads thermal and mechanical allodynia and spontaneous pain. Finally, the psychologic component and neuromodulation cannot be discernibly separated.

Benzon H, Rathmell J, eds. *Raj's Practical Management of Pain*. 4th ed. St. Louis: Mosby; 2008:427–431.

Campbell JN, Raja SN, Meyer RA, et al. Myelinated afferents signal the hyperalgesia associated with nerve injury. *Pain*. 1988;32:89–94.

Payne R. Neuropathic pain syndromes, with special reference to causalgia and reflex sympathetic dystrophy. *Clin J Pain*. 1986;2:59–73.

Pleger B. Patterns of cortical reorganization parallel impaired tactile discrimination and pain intensity in complex regional pain syndrome. *Neuroimage*. 2006;32:503–510.

Wall PD, Melzack R, eds. *Textbook of Pain*. 5th ed. New York: Churchill Livingstone; 2005:1011–1027.

A.9. Define sympathetically maintained pain (SMP) and sympathetically independent pain (SIP).

The pain that is maintained by sympathetic innervation or circulating catecholamines is defined as SMP. It describes a pain mechanism, rather than clinical syndrome. Therefore, by definition, patients with CRPS who report pain relief after a sympathetic block (e.g., stellate ganglion block) have SMP. Conversely, pain conditions that show features of sympathetic overactivity, yet fail to respond to sympathetic blocks, are described as SIP.

Ballantyne JC, Rathmell JP, Fishman SM, eds. *Bonica's the Management of Pain*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:314–331.

Roberts WJ. A hypothesis on the physiologic basis for causalgia and related pains. *Pain*. 1986;24:297–311.

A.10. How does CRPS differ from neuralgia?

The chronic pain seen in neuralgia is usually paroxysmal and follows the distribution of nerve. The pain is sharp and shooting without associated vasomotor or sudomotor changes. The chronic pain syndrome of CRPS is a sustained, diffuse, burning pain independent of nerve distribution and is associated with vasomotor and sudomotor changes.

Benzon H, Rathmell J, eds. *Raj's Practical Management of Pain*. 4th ed. St. Louis: Mosby; 2008:427–431.

A.11. What is central pain? How will you differentiate central pain from CRPS?

Central pain is regional pain initiated or caused by a primary lesion or dysfunction in the central nervous system, usually associated with abnormal sensitivity to temperature and to noxious stimulus. Central pain, also referred to as *deafferentation pain*, is a difficult pain syndrome to treat because the pathophysiology is not well understood. Regional pain not relieved by peripheral nerve blocks, either sympathetic or somatic, is more likely to be central pain. Central pain may be associated with various neurologic symptoms and signs such as monoparesis, hemiparesis, or paraparesis.

Abram SE, Haddox JD, eds. *The Pain Clinic Manual*. 2nd ed. Philadelphia: Lippincott Williams & Wilkins; 2000:253–259.

Ballantyne JC, Rathmell JP, Fishman SM, eds. *Bonica's the Management of Pain*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:314–331.

A.12. Is the social history of this patient relevant to the development of chronic pain?

In patients with CRPS, the disproportionate pain and dysfunction, and the absence of clear pathogenesis and pathophysiology led to examination of potential psychological etiology. Also noted is the fact that as the CRPS progresses, patients' personality mea-

sures such as Minnesota Multiphasic Personality Inventory profiles tend to resemble those of patients experiencing chronic pain and psychological distress as evidenced by hypochondriasis, depression, and hysteria scales. Certainly, stress has been implicated in increasing sympathetic outflow. The literature suggests that the presence of psychological disorders, particularly anxiety and depression, may predispose the patient to the development of CRPS.

Ballantyne JC, Rathmell JP, Fishman SM, eds. *Bonica's the Management of Pain*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:314–331.

Bruehl S, Carlson CR. Predisposing psychological factors in the development of reflex sympathetic dystrophy. *Clin J Pain*. 1992;8:287–299.

Ciccone DS, Bandilla EB, Wen-hsein W. Psychological dysfunction in patients with reflex sympathetic dystrophy. *Pain*. 1997;71:323–333.

B. Pain Management

B.1. How will you work up CRPS types I and II?

CRPS is diagnosed clinically with a detailed history and physical examination. Because it is a clinical diagnosis of exclusion, other specific conditions that could account for the degree of pain and dysfunction must be ruled out. Objective signs are variable but almost universally include loss of function of the affected part as a result of pain. Allodynia and hyperalgesia are extremely common. Change in temperature and sweating may vary depending on the stage of the disease. Several diagnostic studies may aid in the diagnosis of CRPS but are seldom pathognomonic.

A quantitative sweat test may show excessive sweating, and thermography may demonstrate abnormal heat regulation and disparity in temperature between affected and normal regions. Radiologic studies may reveal patchy osteoporosis in early stages. Triple-phase bone scan using technetium-99m may show increased periarticular uptake in the affected extremity. Nevertheless, negative triple-phase bone scan results do not rule out CRPS. Thermographic, radiologic, or scintigraphic findings can be nonspecific and should be correlated with the clinical findings.

Positive diagnostic sympathetic blocks can confirm the sympathetically mediated component of CRPS.

Ballantyne JC, Rathmell JP, Fishman SM, eds. *Bonica's the Management of Pain*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:314–331.

Betcher AM, Casten DF. Reflex sympathetic dystrophy: criteria for diagnosis and treatment. *Anesthesiology*. 1955;6:994–1003.

Merskey H, Bogduk N. Classification of chronic pain. In: Task Force on Taxonomy. International Association for the Study of Pain. *Relatively Generalized Syndromes*. 2nd ed. Seattle: IASP Press; 1994:39–56.

B.2. Describe the sympathetic nerve supply to the arm.

The preganglionic sympathetic outflow to the upper extremity is derived from T2-9. These fibers synapse with postganglionic neurons in the stellate ganglion. Therefore, a stellate ganglion block interrupts sympathetic outflow to the upper extremity.

Benzon H, Rathmell J, eds. *Raj's Practical Management of Pain*. 4th ed. St. Louis: Mosby; 2008:845–846.

B.3. Where is the stellate ganglion located?

The stellate ganglion is formed by the fusion of the inferior cervical and the first thoracic ganglia. It usually measures 2.5 cm × 1.5 cm × 0.5 cm and lies between the base of the transverse process of the seventh cervical vertebra and the neck of the first rib. It is situated behind the carotid sheath, ventral to the longus colli muscle, behind the vertebral artery, and lateral to the body of the vertebra. The vertebral, subclavian, inferior thyroid, and first intercostals arteries are in close proximity to the ganglion, as is the recurrent laryngeal nerve. The left pleura is 1 to 2 cm below it, and the right pleura is in closer proximity.

Benzon H, Rathmell J, eds. *Raj's Practical Management of Pain.* 4th ed. St. Louis: Mosby; 2008:845–846.

Miller RD, ed. *Miller's Anesthesia.* 7th ed. New York: Churchill Livingstone, 2010:1639–1675.

B.4. What are the anatomic landmarks used in the stellate ganglion block?

The landmarks used in the stellate ganglion block are the jugular notch of the sternum, the sternocleidomastoid muscle, the cricoid cartilage, and Chassaignac tubercle. In a supine patient with neck extended, a mark placed approximately 3.5 cm from the midline along the jugular notch and the same distance above the clavicle should overlie the transverse process of the seventh vertebra and the medial border of the sternocleidomastoid muscle. This marking is further confirmed by palpating the cricoid cartilage, which lies at the level of the sixth cervical vertebra, and the anterior tubercle on the vertebral transverse process, which is the most prominent tubercle in the neck (Chassaignac tubercle).

Benzon H, Rathmell J, eds. *Raj's Practical Management of Pain*. 4th ed. St. Louis: Mosby; 2008:845–846.

Miller RD, ed. *Miller's Anesthesia.* 7th ed. New York: Churchill Livingstone; 2010: 1639–1675.

B.5. What are the clinical signs of stellate ganglion block?

A stellate ganglion block results in the following ipsilateral signs:

- *Eye*: Ptosis, narrowing of the palpebral fissure, miosis, enophthalmos, conjunctival injection, and lacrimation
- *Face and neck*: Anhidrosis, elevated local temperature, and nasal stuffiness
- *Arm*: Increased temperature and plethysmographic evidence of improved cutaneous blood flow

Benzon H, Rathmell J, eds. *Raj's Practical Management of Pain*. 4th ed. St. Louis: Mosby; 2008:845–846.

Miller RD, ed. *Miller's Anesthesia.* 7th ed. New York: Churchill Livingstone; 2010:1639–1675.

B.6. What is Horner syndrome?

Horner syndrome is a clinical entity characterized by ptosis, miosis, anhidrosis, and enopthalmos, usually seen with a disease process involving the cervical sympathetics and being the classic signs of a stellate ganglion block.

Benzon H, Rathmell J, eds. *Raj's Practical Management of Pain*. 4th ed. St. Louis: Mosby; 2008:845–846.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. New York: Churchill Livingstone; 2010:1639–1675.

B.7. After a stellate ganglion block, this patient reports no significant change in the degree of pain despite evidence of Horner syndrome. Is the pain psychogenic in this patient?

Not necessarily. Horner syndrome indicates only the interruption of sympathetic supply to the head and neck. Unless it is accompanied by objective changes in the arm, it does not indicate sympathetic nerve block of the upper extremity. Further, SMP will respond to sympathectomy, whereas SIP will not.

Benzon H, Rathmell J, eds. *Raj's Practical Management of Pain*. 4th ed. St. Louis: Mosby; 2008:845–846.

Wall PD, Melzack R, eds. *Textbook of Pain*. 5th ed. New York: Churchill Livingstone; 2005:512.

B.8. What types of nerve fibers are interrupted in stellate ganglion block?

The stellate ganglion block results in interruption of the preganglionic, thinly myelinated type B fibers, as well as the postganglionic, unmyelinated type C fibers.

Ballantyne JC, Rathmell JP, Fishman SM, eds. *Bonica's the Management of Pain*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:314–331.

Casale R, Glynn CJ, Buonocoe M. Autonomic variations after stellate ganglion block: are they evidence of an autonomic afference? *Funct Neurol*. 1990;5:245–246.

B.9. What is a differential block?

The variable effects of local anesthetics on fibers performing different functions are termed *differential block*. The diagnostic distinction can be made by selectively blocking the function of these nerve fibers. The mechanism that results in differential block is best explained by the fiber size and myelination because these factors determine different sensitivities of nerve fibers to local anesthetics. By using different concentrations of local anesthetic, sympathetic and somatic fibers can be selectively blocked. Differential block may be helpful to differentiate somatic versus sympathetic pain and peripheral versus central pain.

Cousins MJ, Bridenbaugh PO, eds. Neural blockade. In: *Clinical Anesthesia and Management of Pain*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:838–840.

B.10. What are the two major classes of local anesthetics? Describe the major differences in their clinical pharmacology.

The two major classes of clinically employed local anesthetics are esters and amides. The esters are hydrolyzed in the plasma by pseudocholinesterase; the amides are biotransformed in the liver. Although infrequent, local anesthetic toxicity is encountered more commonly in the ester group because of the para-aminobenzoic acid

moiety. True allergic reactions to amides are rare and in most instances are caused by preservatives in the solution. The two groups of local anesthetics contain drugs with varying degrees of rate of onset, duration of neural blockade, potency, and toxicity.

Benzon H, Rathmell J, eds. *Raj's Practical Management of Pain*. 4th ed. St. Louis: Mosby; 2008:811–839.

B.11. What factors determine the onset, potency, and duration of a local anesthetic block?

- Onset correlates with pK_a
- Potency correlates with lipid solubility
- Duration correlates with degree of protein binding

The commonly used local anesthetics are weakly basic tertiary amines that are lipid soluble and unstable in water. They are prepared as acidic salts because the ionized form, which is soluble in water, is stable. Therefore, the aqueous solution contains the ionized (cation) form of the local anesthetic in dissociation equilibrium with the unionized (free base) form, depending on the pH of the medium.

$$\underset{\text{Cation}}{R \equiv NH^+} \rightleftharpoons \underset{\text{Base}}{R \equiv N} + H^+$$

When the local anesthetic is injected into the body, the relative rise in pH will allow the local anesthetic to convert to the uncharged base. The free base, being lipid soluble, will diffuse across the neural membrane and is responsible for neural blockade. With the exception of procaine and chloroprocaine, the commonly employed local anesthetics are highly protein bound, and are therefore longer acting (Table 47.1).

Cousins MJ, Bridenbaugh PO, eds. Neural blockade. In: *Clinical Anesthesia and management of Pain*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:26–48.

Benzon H, Rathmell J, eds. *Raj's Practical Management of Pain*. 4th ed. St. Louis: Mosby; 2008:811–839.

Table 47.1 Physiochemical Properties of Commonly Used Local Anesthetics

LOCAL ANESTHETIC	pK_A	PROTEIN BINDING (%)
Esters		
Procaine	8.9	5.8
Chloroprocaine	8.7	—
Tetracaine	8.5	75.6
Amides		
Lidocaine	7.9	64.3
Mepivacaine	7.6	77.5
Bupivacaine	8.1	95.6
Etidocaine	7.7	94.0

B.12. How does the addition of epinephrine to commercially available premixed solutions affect the efficacy of local anesthetics?

The addition of epinephrine to a local anesthetic increases the duration and intensity of a block. In commercially available premixed solutions containing epinephrine, antioxidants are added to preserve epinephrine and the result is a lower buffered pH level of the solution. This lowering of the pH level can result in decreased efficacy of the local anesthetic. Best results are achieved by adding the desired concentration of epinephrine to the local anesthetic solution just before injection.

Benzon H, Rathmell J, eds. *Raj's Practical Management of Pain*. 4th ed. St. Louis: Mosby; 2008:811–839.

Mooer DC. The pH of local anesthetic solutions: technical communication. *Anesth Analg*. 1981;60:833–834.

B.13. How will you treat this patient?

Early diagnosis and aggressive physical therapy with pharmacologic control of pain form the basis of the treatment of CRPS. Physical therapy is widely recommended and accepted as a first line of treatment. The treatment of CRPS will differ depending on whether the pain is sympathetically maintained pain (SMP) or SIP. A series of sympathetic blocks has been shown effective in treating SMP of CRPS. A multidisciplinary approach including physiotherapy and symptom-specific psychological treatments (e.g., biofeedback and hypnosis) may be beneficial. Many patients have a component of both SMP and SIP, and a combination of sympathectomy and analgesic treatment is recommended. Nevertheless, no single treatment is consistently successful. Therefore, the treatment plan should be individualized.

Ballantyne JC, Rathmell JP, Fishman SM, eds. *Bonica's the Management of Pain*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:314–331.

Wall PD, Melzack R, eds. *Textbook of Pain*. 5th ed. New York: Churchill Livingstone; 2005:1011–1027.

B.14. What is the pharmacologic management of CRPS?

SMP of CRPS is treated with the drugs that deplete norepinephrine from the sympathetic nerve terminals. Oral sympatholytic agents include phenoxybenzamine, prazosin, and terazosin. Topical clonidine, a selective α_2-agonist, has been successfully used to treat SMP. Tricyclic antidepressants have been effective in approximately half the number of patients and have been recommended as first-line agents. Other drugs that have been successfully used to treat CRPS are anticonvulsants (e.g., gabapentin, pregabalin, carbamazepine, and topiramate), local anesthetics such as lidocaine and mexiletine, calcitonin, corticosteroids, and high-dose opioids. Anecdotal reports suggest that methadone (opioid with anti-NMDA receptor effect) has been more effective than other opioids. Long-term intrathecal morphine has been reported to produce analgesic effects in CRPS. Nonsteroidal anti-inflammatory drugs have also been used successfully.

Abram SE, Haddox JD, eds. *The Pain Clinic Manual*. Philadelphia: Lippincott Williams & Wilkins; 2001:177–184.

Ballantyne JC, Rathmell JP, Fishman SM, eds. *Bonica's the Management of Pain*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:314–331.

Becker WJ, Ablett DP, Harris CJ, et al. Long-term treatment of intractable reflex sympathetic dystrophy with intrathecal morphine. *Can J Neurosci*. 1995;22:153–159.

B.15. What is the role of intravenous regional block (Bier method) in diagnosis and treatment of CRPS?

Intravenous regional block (Bier method) with guanethidine, reserpine, bretylium, and phentolamine has been used to achieve temporary sympatholytic effect and relieve sympathetically maintained pain (SMP) of CRPS. Intravenous guanethidine and reserpine have been reported to relieve pain in more than 50% of patients compared with a control group in one study. Nevertheless, guanethidine and reserpine are not commercially available in the United States. The combination of bretylium and lidocaine is more effective than lidocaine alone. α-Adrenergic blockade with intravenous phentolamine is a sensitive test to identify patients with SMP. Phentolamine has been used as a predictor agent before more invasive sympathetic blocks.

Ballantyne JC, Rathmell JP, Fishman SM, eds. *Bonica's the Management of Pain*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:314–331.

Blanchard J, Ramamurthy S, Walsh N, et al. Intravenous regional sympatholysis: a double blind comparison guanethidine, reserpine and normal saline. *J Pain Symptom Manage*. 1990;5:357–361.

Hord AH, Rooks MD, Stephens BO, et al. Intravenous regional bretylium and lidocaine for the treatment of reflex sympathetic dystrophy: a randomized double blind study. *Reg Anesth Pain Med*. 1992;74:818–821.

Raja SN, Treede RD, Davis KD, et al. Systemic alpha-adrenergic blockade with phentolamine: a diagnostic test for sympathetically maintained pain. *Anesthesiology*. 1991;74:691–698.

B.16. Compare and contrast the mechanism of action of ketamine and methadone.

Methadone is a strong, long-acting opioid analgesic; ketamine is a dissociative anesthetic. Methadone is used as an opioid, but has mild N-methyl-D-aspartate (NMDA) receptor antagonist properties and is the only strong opioid that has this quality. Ketamine is used in oral preparations, intravenous delivery systems, skin preparations, and other delivery methods, including being compounded in various percentages. These medications can block NMDA receptors and decrease the windup pain and central sensitization typical of chronic intractable pain. Windup causes an amplification of the incoming pain signal at the level of second-degree neurons in the dorsal horn of the spinal cord. By blocking these receptors, not only is windup pain decreased, but tolerance to opioid medications can also be decreased. Ketamine has the added effect of blocking sodium channels.

Benzon H, Rathmell J, eds. *Raj's Practical Management of Pain*. 4th ed. St. Louis: Mosby; 2008:300,605–606.

Chizh, B. Low dose ketamine: a therapeutic and research tool to explore N-methyl-D-aspartate (NMDA) receptor-mediated plasticity in pain pathways. *J Psychopharmacol*. 2007;21:259–271.

B.17. What role does ketamine infusion play in the treatment of CRPS?

Although ketamine may have more than one mechanism of action, the basis for using it to treat CRPS may reside in its strong ability to block NMDA receptors. Ketamine is the only potent NMDA-blocking drug currently available for clinical use. An appropriately prolonged infusion of ketamine appears to maintain a level of ketamine in the

central nervous system long enough to reverse the effects of the sensitization process and associated pain.

Currently, three methods of ketamine administration have been used for treatment, including an outpatient low-dose ketamine administration, a low-dose awake inpatient technique, and a ketamine "coma" technique, a more controversial treatment not currently allowed in the United States. While studies are continuing, intravenous ketamine therapy has been shown to be effective for relief of pain in CRPS-I. There were no adverse cognitive effects of extended treatment with ketamine infusion. Side effects, nevertheless, can occur in the high dose setting, because the infusion can be associated with significant risks, including endotracheal intubation and chronic catheterization with the need for parenteral nutrition. The outpatient therapy requires the patient to return for a 10-day period and often showed loss of effectiveness after 6 to 12 weeks.

Ballantyne JC, Rathmell JP, Fishman SM, eds. *Bonica's the Management of Pain*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:314–331.

Goldberg ME, Torjman MC, Schwartzman RJ, et al. Pharmacodynamic profiles of ketamine (R)- and (S)- with 5-day inpatient infusion for the treatment of complex regional pain syndrome. *Pain Physician*. 2010;13:379–387.

Kiefer R, Rohr P, Ploppa A, et al. Complete recovery from intractable complex regional pain syndrome, CRPS-type I, following anesthetic ketamine and midazolam. *Pain Pract*. 2007;7:147–150.

B.18. What is the role of spinal cord stimulation (SCS) and surgical sympathectomy?

Surgical, chemical, or radiofrequency sympathectomies produces short-term pain relief, but long-term results are poor and inconsistent. Delayed failure of sympathectomy may be due to regeneration of ipsilateral nerves or reinnervation from the contralateral sympathetic nerves. SCS is an effective treatment for the pain of CRPS, including recurrent pain after surgical or radiofrequency sympatholysis. Epidural SCS is a simple procedure and carries low morbidity.

Ballantyne JC, Rathmell JP, Fishman SM, eds. *Bonica's the Management of Pain*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:314–331.

Kumar K, Nath RK, Toth C. Spinal cord stimulation is effective in the management of reflex sympathetic dystrophy. *Neurosurgery*. 1997;40:503–508.

Rocco AG. Radiofrequency lumbar sympatholysis: the evolution of a technique for managing sympathetically maintained pain. *Reg Anesth*. 1995;20:3–12.

C. Complications

C.1. What are the complications of stellate ganglion block?

Although complications appear infrequently, the more common complications of stellate ganglion block are as follows:

- Intra-arterial injection: Seizure and hematoma
- Recurrent laryngeal nerve paralysis: Hoarseness of voice
- Brachial plexus block: Motor weakness
- Accidental epidural or subarachnoid injection
- Esophageal injury
- Pneumothorax: Respiratory distress

To avoid complications, aspiration of the needle should be performed before, during, and after administration of local anesthetics to look for (1) air, (2) blood, and (3) cerebrospinal fluid.

Benzon H, Rathmell J, eds. *Raj's Practical Management of Pain*, 4th ed. St. Louis: Mosby; 2008:851–889.

Miller RD, ed. *Anesthesia*. 7th ed. New York: Churchill Livingstone; 2009:1639–1675.

C.2. What is the systemic toxicity of local anesthetics?

The systemic toxic effects of local anesthetics are related to drug levels in blood and are manifested mainly in the central nervous system and the cardiovascular system. As a rule, the central nervous system effects precede the cardiovascular toxic manifestations.

Central nervous system effects

Central nervous system include light-headedness, dizziness, tinnitus, visual disturbances, drowsiness, disorientation, slurred speech, muscle twitching, generalized grand mal seizures, and electroencephalographic changes. Blood levels of local anesthetics associated with central nervous system changes in humans are as follows:

- Procaine: 20 μg per mL
- Lidocaine, mepivacaine, and prilocaine: 5 to 10 μg per mL
- Tetracaine, bupivacaine, and etidocaine: 1.5 to 4 μg per mL
- Lowering the $Paco_2$ by hyperventilation decreases the seizure threshold dose of a local anesthetic drug.

Cardiovascular effects

Ventricular arrhythmias are reported with intravenous bupivacaine only. Cardiac resuscitation is extremely difficult in patients with bupivacaine-induced cardiac arrhythmias. Ropivacaine is less toxic than bupivacaine but more toxic than lidocaine. The mechanism of enhanced cardiotoxicity in pregnant patients is not well understood; nevertheless, 0.75% bupivacaine is no longer recommended in pregnant patients in the United States (Table 47.2).

Table 47.2 Cardiovascular Effects of Lidocaine

BLOOD LEVEL LIDOCAINE (μg/mL)	ELECTROCARDIOGRAPHIC CHANGES	HEMODYNAMIC EFFECTS
<5	–	–
5–10	↑ PR interval	↓ Myocardial contraction
	↑ QRS duration	↓ Cardiac output
	Sinus bradycardia	Vasodilatation
>10	↑ PR interval	↓ Myocardial contraction
	↑ QRS duration	↓ Cardiac output
	Sinus bradycardia	Circulatory collapse
	Atrioventricular block	
	Asystole	

↑, increase; ↓, decrease.

Benzon H, Rathmell J, eds. *Raj's Practical Management of Pain*. 4th ed. St. Louis: Mosby; 2008:811–839.

Cousins MJ, Bridenbaugh PO, eds. Neural blockade. In: *Clinical Anesthesia and Management of Pain*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:114–133.

Miller RD, ed. *Anesthesia*. 7th ed. New York: Churchill Livingstone; 2009:913–941.

C.3. How do you treat the systemic toxicity of local anesthetic drugs?

The principles of treatment include the following:

- Secure and maintain the airway.
- Ensure adequate oxygenation and ventilation.
- Treat hypotension and bradycardia promptly.
- Perform immediate cardiopulmonary resuscitation for profound cardiovascular collapse.
- Perform electrical cardioversion for ventricular tachycardia or fibrillation.
- Control seizures with the following:
  - Midazolam 2 to 5 mg intravenously
  - Thiopental sodium 1 to 2 mg per kg intravenously
  - Propofol 1 to 2 mg per kg intravenously
- Administer intravenous lipid to remove bupivacaine from sites of action. Administration of 100 mL of 20% lipid solution has been reported to successfully resuscitate a patient from bupivacaine-induced dysrhythmias refractory to conventional therapy.

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:544–545.

Benzon H, Rathmell J, eds. *Raj's Practical Management of Pain*. 4th ed. St. Louis: Mosby; 2008:811–839.

Cousins MJ, Bridenbaugh PO, eds. Neural blockade. In: *Clinical Anesthesia and Management of Pain*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:114–133.

Miller RD, ed. *Anesthesia*. 7th ed. New York: Churchill Livingstone; 2009:1611–1639.

Weinberg G. Lipid infusion resuscitation for local anesthetic toxicity: proof of clinical efficacy. *Anesthesiology*. 2006;105:7–8.

CHAPTER 48

Cancer Pain

Sudhir A. Diwan, Shakil Ahmed, and Neel D. Mehta

A 44-YEAR-OLD MAN

was referred to the pain clinic for evaluation and management of abdominal pain. He was recently diagnosed with adenocarcinoma of pancreas with retroperitoneal lymph nodes in the para-aortic region. His pain was localized in the epigastric region and was worse during the night and decreased during the day. He was taking sustained-release morphine sulfate (MS Contin), 100 mg orally every 8 hours, and immediate-release morphine sulfate, 30 mg orally every 3 hours as needed, for breakthrough pain. The patient reported inadequate pain control, nausea, vomiting, and constipation.

A. Medical Disease and Differential Diagnosis

1. What is the definition of pain?
2. How significant is the problem of pain in patients with cancer?
3. What are the components of cancer pain?
4. How does pain contribute to the suffering of patients with cancer?
5. How do psychological factors affect pain in patients with cancer?
6. What are the causes of pain in patients with cancer?
7. How do you classify pain in patients with cancer?
8. What are the characteristics of pancreatic cancer pain?
9. How do you assess pain in patients with cancer?
10. What is the differential diagnosis of abdominal pain?

B. Pharmacologic Treatment of Pain

1. What is the World Health Organization (WHO) stepladder approach for cancer pain management?
2. Which class of drugs does morphine sulfate belong to?
3. What is the difference between morphine and synthetic opioids?
4. How does a mixed opioid agonist/antagonist differ from an opioid agonist?

5. Describe the role of methadone in the management of cancer pain.
6. What are the advantages and disadvantages of methadone?
7. What is the mechanism of action of opioids?
8. What are the side effects of opioid therapy?
9. Define tolerance and physical dependence.
10. How would you treat the side effects of opioid therapy?
11. What is tramadol? Is it an opiate? What is tapentadol and how does it compare to traditional opiates?
12. When would you consider adjuvant analgesics as part of the treatment plan?
13. The patient and his family are worried about addiction. How would you approach this problem?
14. Describe different routes of opioid administration.
15. Describe advantages and complications of patient-controlled analgesia (PCA). What is minimum effective analgesic concentration (MEAC)?
16. What is meperidine? How is it different from other opioids?
17. What is rotation of opioids? When would you consider rotation of opioids?

C. Invasive Therapy

1. Describe the role of peripheral nerve blocks in cancer pain management.
2. Describe the role of a celiac plexus block in cancer pain management.
3. What are the complications of celiac plexus block?
4. Would you consider neuraxial opioid infusion in this patient? Discuss complications of this procedure.
5. Which medications can be used intrathecally? What is ziconotide?
6. What is a Personal Therapy Manager (PTM) and what role does it play in neuraxial pain relief?
7. Would you consider neuraxial neurolysis in this patient to manage his pain? Discuss advantages and disadvantages of these blocks.
8. Which neuroablative procedures can be considered in the terminal stage of pancreatic cancer?
9. Describe the role of radiation therapy in cancer pain.

D. Nonpharmacologic Management

1. What are the various nonpharmacologic techniques of cancer pain management?
2. What physical modalities have been successfully tried in cancer pain management?
3. Describe the role of neuromodulation in cancer pain management.
4. What psychological techniques have been promoted for comfort care and pain relief?
5. What are distraction and reframing techniques? What is the role of hypnosis in cancer pain management?

A. Medical Disease and Differential Diagnosis

A.1. What is the definition of pain?

According to the International Association of the Study of Pain, pain is defined as "an unpleasant, sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage."

Merskey H, Bogduk N, eds. *Classification of Chronic Pain: Descriptions of Chronic Pain Syndromes and Definitions of Pain Terms*. 2nd ed. Seattle: IASP Press; 1994:210.

A.2. How significant is the problem of pain in patients with cancer?

There are 1,382,400 new patients with cancer annually. Cancer causes 560,000 deaths per year, making it the second leading cause of death in the United States. Thirty percent of the patients with cancer have pain at the time of diagnosis, and 65% to 85% of patients with cancer have pain at advanced stages. Of these, 36% have pain severe enough to impair their ability to function.

Vainio et al. studied 1,840 patients with advanced cancer and found 24% with no pain, 24% with mild pain, 30% with moderate pain, and 21% with severe pain. Daut and Cleeland found pain to be an early symptom of cancer in 48% to 50% of patients with cancer of breasts, ovary, prostate, colon, and rectum, and in 20% of patients with uterus and cervical cancer.

It is estimated that 43,140 men and women (21,370 men and 21,770 women) will be diagnosed with pancreatic cancer and 36,800 men and women will die of the disease in 2010. WHO estimates that 25% of all cancer patients die with unrelieved pain (Table 48.1).

American Cancer Society. *Cancer Facts & Figures—2010*. Atlanta: American Cancer Society; 2010.

Bruera E, Kim H. Cancer pain. *JAMA*. 2003;209:2476–2479.

Hewitt D. The management of pain in the oncology patient. *Obstet Gynecol Clin*. 2001; 28:819–846.

A.3. What are the components of cancer pain?

The components of cancer pain are sensory, affective, and psychological. The sensory components could be nociceptive pain elicited by activation of sensory nerve endings by mechanical, chemical, radioactive, or thermal energy. It is often associated with ongoing tissue damage and may be of somatic or visceral origin. Somatic pain may be superficial, well localized, sharp, pricking, burning or deep diffused, dull, and aching. Visceral pain is usually diffuse, referred to body surface, and has a sickening quality to it.

Neuropathic pain is due to pathologic change in the discharge properties of the neurons because of invasion, compression, or damage caused by various cancer treatment modalities. It is typically described as burning, lancinating, painful numbness, or itching sensations. Phantom pain is a pain referred to the amputated part of the body. Psychological pain is usually due to fear, anxiety, depression, existential questions, anger, social and financial issues, social support, and the impact the pain has on the family and caregivers. Most cancer patients report more than one site of pain.

Ballantyne JC, Fishman SM, Rathmell JPC, et al., eds. *Bonica's Management of Pain*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:537–559.

Sela RA, Bruera E, Conner-Spady B, et al. Sensory and affective dimensions of advanced cancer pain. *Psychooncology*. 2002;11:23–34.

Zaza C, Baine N. Cancer pain and psychosocial factors: a critical review of the literature. *J Pain Symptom Manage*. 2002;24:526–542.

Table 48.1 Estimated New Cancer Cases and Deaths for 2010, All Races, By Sex

	ESTIMATED NEW CASES			ESTIMATED DEATHS		
PRIMARY SITE	TOTAL	MALES	FEMALES	TOTAL	MALES	FEMALES
All sites	1,529,560	789,620	739,940	569,490	299,200	270,290
Oral cavity and pharynx	36,540	25,420	11,120	7,880	5,430	2,450
Tongue	10,990	7,690	3,300	1,990	1,300	690
Mouth	10,840	6,430	4,410	1,830	1,140	690
Pharynx	12,660	9,880	2,780	2,410	1,730	680
Other oral cavity	2,050	1,420	630	1,650	1,260	390
Digestive system	274,330	148,540	125,790	139,580	79,010	60,570
Esophagus	16,640	13,130	3,510	14,500	11,650	2,850
Stomach	21,000	12,730	8,270	10,570	6,350	4,220
Small intestine	6,960	3,680	3,280	1,100	610	490
Colon[a]	102,900	49,470	53,430	51,370	26,580	24,790
Rectum	39,670	22,620	17,050			
Anus, anal canal, and anorectum	5,260	2,000	3,260	720	280	440
Liver and intrahepatic Bile duct	24,120	17,430	6,690	18,910	12,720	6,190
Gallbladder and other biliary	9,760	4,450	5,310	3,320	1,240	2,080
Pancreas	43,140	21,370	21,770	36,800	18,770	18,030
Other digestive	4,880	1,660	3,220	2,290	810	1,480
Respiratory system	240,610	130,600	110,010	161,670	89,550	72,120
Larynx	12,720	10,110	2,610	3,600	2,870	730
Lung and bronchus	222,520	116,750	105,770	157,300	86,220	71,080
Other respiratory	5,370	3,740	1,630	770	460	310
Bones and joints	2,650	1,530	1,120	1,460	830	630
Soft tissue	10,520	5,680	4,840	3,920	2,020	1,900
Skin (excl. basal and squamous)	74,010	42,610	31,400	11,790	7,910	3,880
Melanoma of the skin[b]	68,130	38,870	29,260	8,700	5,670	3,030
Other nonepithelial skin	5,880	3,740	2,140	3,090	2,240	850
Breast[b]	209,060	1,970	207,090	40,230	390	39,840
Genital organs	311,210	227,460	83,750	60,420	32,710	27,710
Cervix (uterus)	12,200		12,200	4,210		4,210
Endometrium (uterus)	43,470		43,470	7,950		7,950
Ovary	21,880		21,880	13,850		13,850

(Continued)

Table 48.1 Estimated New Cancer Cases and Deaths for 2010, All Races, By Sex *(cont.)*

PRIMARY SITE	ESTIMATED NEW CASES			ESTIMATED DEATHS		
	TOTAL	MALES	FEMALES	TOTAL	MALES	FEMALES
Vulva	3,900		3,900	920		920
Vagina and other genital organs, female	2,300		2,300	780		780
Prostate	217,730	217,730		32,050	32,050	
Testis	8,480	8,480		350	350	
Penis and other genital organs, male	1,250	1,250		310	310	
Urinary system	131,260	89,620	41,640	28,550	19,110	9,440
Urinary bladder	70,530	52,760	17,770	14,680	10,410	4,270
Kidney and renal pelvis	58,240	35,370	22,870	13,040	8,210	4,830
Ureter and other urinary organs	2,490	1,490	1,000	830	490	340
Eye and orbit	2,480	1,240	1,240	230	120	110
Brain and other nervous system	22,020	11,980	10,040	13,140	7,420	5,720
Endocrine system	46,930	11,890	35,040	2,570	1,140	1,430
Thyroid	44,670	10,740	33,930	1,690	730	960
Other endocrine	2,260	1,150	1,110	880	410	470
Lymphoma	74,030	40,050	33,980	21,530	11,450	10,080
Hodgkin lymphoma	8,490	4,670	3,820	1,320	740	580
Non-Hodgkin lymphoma	65,540	35,380	30,160	20,210	10,710	9,500
Myeloma	20,180	11,170	9,010	10,650	5,760	4,890
Leukemia	43,050	24,690	18,360	21,840	12,660	9,180
Lymphocytic leukemias	20,320	12,020	8,300	5,810	3,440	2,370
Myeloid leukemias	17,200	9,390	7,810	9,390	5,470	3,920
Other leukemia	5,530	3,280	2,250	6,640	3,750	2,890
All other sites[c]	30,680	15,170	15,510	44,030	23,690	20,340

Cancer Facts & Figures – 2010, American Cancer Society (ACS), Atlanta, Georgia, 2010.
Excludes basal and squamous cell skin and in situ carcinomas except urinary bladder.
Incidence projections are based on rates from the North American Association of Central Cancer Registries (NAACCR) from 1995–2006, representing about 89% of the US population.
Estimated deaths are based on data from US Mortality Data, 1969–2007, National Center for Health Statistics, Centers for Disease Control and Prevention, 2010.
[a] Estimated deaths for colon and rectum cancers are combined.
[b] Carcinoma in situ of the breast accounts for about 54,010 new cases annually, and melanoma in situ accounts for about 46,770 new cases annually.
[c] More deaths than cases suggests lack of specificity in recording underlying causes of death on death certificate.

A.4. How does the pain contribute to the suffering of patients with cancer?

Sustained pain on its own can create complex, enduring, unpleasant emotional suffering by its ability to create awareness of the perceived threat to one's life. It causes helplessness in the face of the inevitability of demise as well as exhaustion of hope. Patients with cancer usually identify pain as an indicator of disease progression. Suffering may be attributable to many factors besides physical complaints. Psychological factors include financial issues, lack of social support, loss of job or social position in society, loss of independence, effect on family and friends, social isolation, and fear of death.

Speigel D, Giese-Davis J. Depression and cancer pain: mechanisms and disease progression. *Biol Psychiatry.* 2003;54:269–282.

A.5. How do psychological factors affect pain in patients with cancer?

The ultimate perception of pain depends on the nociceptive stimulus and psychological fear, anger, anxiety, or depression. Twenty-five percent of patients with cancer meet criteria for major depressive syndromes at some point in their illness, with an overall prevalence of 53% in hospitalized patients with cancer. Psychological factors may significantly exacerbate pain. Symptoms usually include anxiety, restlessness, irritability, sleep disorders, obsessive thinking, slowness in motor responses, and hopelessness. These factors affect overall pain behavior and suffering.

Speigel D, Giese-Davis J. Depression and cancer pain: mechanisms and disease progression. *Biol Psychiatry.* 2003;54:269–282.

A.6. What are the causes of pain in patients with cancer?

Pain in patients with cancer may be due to (1) presence and progression of the tumor itself, for example, bone involvement, viscus obstruction, and nerve compression; (2) indirect effect of the tumor, for example, metabolic imbalance, infection, and venous or lymphatic obstruction; (3) consequence of cancer treatment, such as chemotherapy, radiation therapy, or surgery; or (4) unrelated mechanisms such as migraine and myofascial pain.

Localized invasion of peripancreatic structures most commonly causes back pain, which stems from tumor invasion of the splanchnic plexus, common bile duct obstruction, retroperitoneum, or pancreatitis. This pain is described as severe, gnawing, epigastric, upper abdominal radiating to the middle of the back, worse on lying down and improved with upright position.

Grond et al. found in a prospective study of 2,266 patients with cancer that 30% had one pain syndrome, 39% had two pain syndromes, 31% had three pain syndromes, 85% by the cancer itself (bone, 35%; soft tissue, 45%; and visceral, 34%), and 17% by anticancer treatment.

Ballantyne JC, Fishman SM, Rathmell JP, et al., eds. *Bonica's Management of Pain.* 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:537–559.

Cherny N. The management of cancer pain. *CA Cancer J Clin.* 2000;50:70–116.

A.7. How do you classify pain in patients with cancer?

Pain, in patients with cancer, may be classified on the basis of the following:

- Chronicity: acute or chronic
- Intensity and severity: visual analog score, numeric pain score, and verbal: mild, moderate, severe, or worst possible pain

- Pathophysiology and mechanism: nociceptive or neuropathic; tumor infiltration of nerves; infiltration of soft tissue or hollow organs, serosa, solid organ necrosis; and destruction of bone
- Individual type and stage of disease: pancreatic, ovarian, prostatic, breast, or lung
- Pattern of pain: incidental pain related to an event or activity; spontaneous pain unrelated to an event or activity and end-of-dose failure
- Pain syndromes: tumor invasion of bone, nerves, spinal cord, viscera, blood vessels, postsurgical, and postchemotherapy and postradiation therapy pain

The pancreatic carcinoma usually presents with vague symptoms of anorexia, weight loss, abdominal discomfort, new-onset diabetes mellitus, or thrombophlebitis. The vague nature of symptoms may result in the delay of diagnosis

Caraceni A, Weinstein S. Classification of cancer pain syndromes. *Oncology*. 2001;15: 1627–1640.

A.8. What are the characteristics of pancreatic cancer pain?

Pancreatic cancer affects 9 or 10 patients per 100,000 in the Western world, men more than women, and blacks more than whites. From 2003 to 2007, the median age at diagnosis for cancer of the pancreas was 72 years of age. The overall 5-year relative survival for 1999 to 2006 from 17 Surveillance, Epidemiology, and End Results geographic areas was 5.6%. Five-year relative survival by race and sex was 5.4% for white men, 5.7% for white women, 4.2% for black men, and 6.0% for black women. Approximately 30% to 60% of patients present with pain, and 80% of the patients with advanced cancer complain of pain. Patients complain of diffuse epigastric pain radiating to the back that is increased on lying down and improved on sitting. About 90% of pancreatic tumors are of the adenocarcinoma type. Cancer in the head of the pancreas usually invades the stomach, duodenum, gallbladder, and peritoneum, whereas tumors in the body spread to liver, spleen, lymph nodes, and left adrenal gland.

Altekruse S, Kosary C, Krapcho M, et al., eds. *SEER Cancer Statistics Review, 1975–2007*. Bethesda, MD: National Cancer Institute. Available at: http://seer.cancer.gov/csr/1975_2007.

Hawes R, Xiong Q, Waxman I, et al. A multispecialty approach to the diagnosis and management of pancreatic cancer. *Am J Gastoenterol*. 2000;95:17–31.

A.9. How do you assess pain in patients with cancer?

A stepwise approach is required for the assessment of pain. It includes history, physical examination, and data collection and ends with clinical diagnosis. It helps the clinician achieve goals of providing pain relief. Assessment involves identifying features of pain, such as location, intensity, quality, timing, exacerbating and relieving factors, response to previous analgesics, and disease-modifying treatments; effects of pain on daily activities and psychological state; associated symptoms; complete physical examination; and laboratory data and imaging.

Ballantyne JC, Fishman SM, Rathmell JP, et al., eds. *Bonica's Management of Pain*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:559–635.

A.10. What is the differential diagnosis of abdominal pain?

Although abdominal pain could arise from different structures within the peritoneal cavity, the retroperitoneal organs can cause similar pain syndromes. Location and

radiation of the pain can give important clues to make the diagnosis. Retroperitoneal structures present with dull or sharp back pain that is increased on lying down and relieved on sitting hunched up. Abdominal tumors are frequently characterized by colicky pain associated with nausea that is worse after eating. Abdominal pain may be referred to distant areas such as the shoulder, neck, or back, depending on the organ involved. Tumors of the small bowel or large bowel may present with symptoms of obstruction (e.g., abdominal distention, nausea, bilious vomiting) or hematemesis or melena. Other common causes of abdominal pain include omental metastasis, volvulus of intestine, infectious peritonitis, radiation enteritis, and peritoneal carcinomatosis. Mesenteric ischemia presents with diffuse pain that is increased with meals and weight loss.

Nonmalignant causes of abdominal pain such as appendicitis, cholecystitis, and pancreatitis can occur in patients with cancer coincidentally and may complicate the diagnostic process. Opioid analgesics may not be used in these patients because they may exacerbate symptoms of colicky pain (resulting from spasm of sphincter of Oddi), nausea, vomiting, paralytic ileus, and constipation.

Ballantyne JC, Fishman SM, Rathmell JP, et al., eds. *Bonica's Management of Pain*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:899–925.

B. Pharmacologic Treatment of Pain

B.1. What is the World Health Organization (WHO) stepladder approach for cancer pain management?

The WHO advocated a stepladder approach to manage cancer pain exclusively with oral medications depending on the pain intensity and to some extent the pain mechanism (Fig. 48.1).

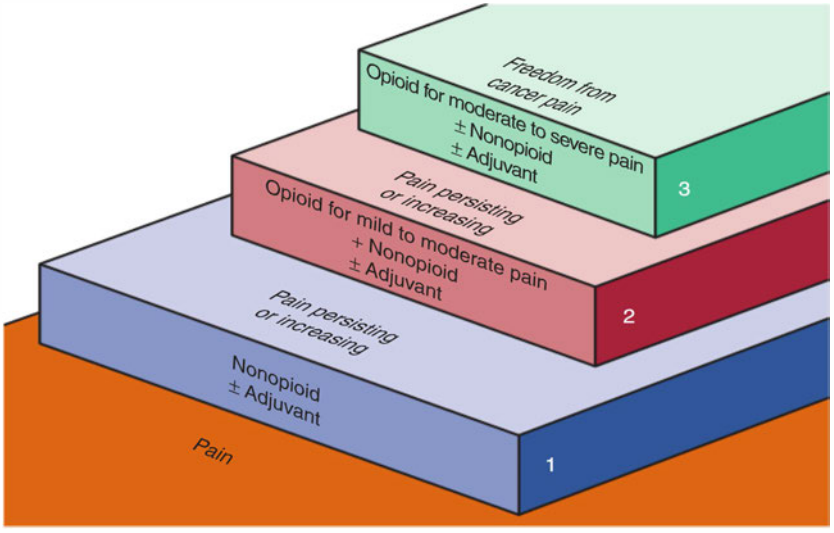


Figure 48.1 World Health Organization–advocated stepladder approach to management of cancer pain.

Step 1. Manage the pain by nonopioid medications with or without adjuvants.
Step 2. If pain is persisting or increasing, add weak opioids to nonopioid analgesics and adjuvants.
Step 3. Strong opioids are used with nonopioid analgesics and adjuvants until the patient achieves complete analgesia.

At this point, if pain still persists, neurolytic or interventional procedures should be employed. Noninvasive routes of drug delivery should be maintained as long as possible, because of its simplicity, convenience, and cost.

Abram S, Haddox J, eds. *The Pain Clinic Manual*. 2nd ed. Philadelphia: Lippincott Williams & Wilkins; 2000:293–351.

Pazdur R, Wagman L , Camphausen KA, et al., eds. *Cancer Management: A Multidisciplinary Approach*. 12th ed. Philadelphia: F.A. Davis Company; 2010:731–746.

B.2. Which class of drugs does morphine sulfate belong to?

Morphine is classified as a μ-receptor opioid agonist because of its high specificity for activation of μ-receptors. An ideal opioid agonist would have a high specificity for receptors producing desirable effects (analgesia and minimal or no specificity for other receptors that cause side effects). Opioids are unique in producing analgesia without loss of consciousness.

Brunton L, Chabner B, Knollman B. *Goodman and Gilman's The Pharmacological Basis of Therapeutics*. 12th ed. New York: McGraw-Hill; 2011:566–578.

B.3. What is the difference between morphine and synthetic opioids?

Morphine is the principal phenanthrene alkaloid present in opium. It is highly ionized and water-soluble. The most active molecule of morphine is the levorotatory isomer of stereochemical structure. The synthetic opiates contain the phenanthrene nucleus of morphine and are manufactured by synthesis, rather than chemical modification. Clinically, histamine release by morphine differentiates it from the synthetic opioids. This may cause urticaria, allergic reactions, and hemodynamic instability, particularly in volume-depleted patients.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:769–824.

B.4. How does a mixed opioid agonist/antagonist differ from an opioid agonist?

The mixed-action opioids bind to μ-receptors, where they are partial agonists or competitive antagonists. Antagonistic properties of these drugs can attenuate the efficacy of subsequently administered opioid agonists and cause withdrawal symptoms in patients already receiving opioid agonists. The advantages of these drugs include low potential for respiratory depression and physical dependence. A dysphoric reaction is very common with mixed-action opioids. Their use is limited because of a ceiling effect, whereby progressive escalation in doses does not increase analgesia as with opioid agonists.

Brunton L, Chabner B, Knollman B. *Goodman and Gilman's The Pharmacological Basis of Therapeutics*. 12th ed. New York: McGraw-Hill; 2011:566–578.

B.5. Describe the role of methadone in the management of cancer pain.

The efficient oral and rectal absorption with prolonged duration of analgesic action of methadone makes it a highly effective and attractive oral drug for cancer pain management. Methadone is a synthetic opiate drug with a unique agonist/antagonist action. Methadone is a μ-receptor agonist and an *N*-methyl-D-aspartate (NMDA) receptor antagonist. Activation of NMDA receptors is involved in the development of hypersensitivity and central sensitization in neuropathic pain and tolerance to opioids. Because of the antagonistic effect at the NMDA receptor site, methadone is very effective in neuropathic pain secondary to cancer-related pathology and therapeutic interventions. The same antagonistic action of methadone minimizes the development of tolerance to opioids.

Brunton L, Chabner B, Knollman B. *Goodman and Gilman's The Pharmacological Basis of Therapeutics*. 12th ed. New York: McGraw-Hill; 2011:566–578.

Manfredi PL, Gonzalez GR, Cheville AL, et al. Methadone analgesia in cancer patients on chronic methadone maintenance therapy. *J Pain Symptom Manage*. 2001;21:169–174.

B.6. What are the advantages and disadvantages of methadone?

Methadone has several advantages, including oral and rectal absorption with bioavailability to 95%, high potency, high lipid solubility, low cost, and no active metabolites. Methadone has a long half-life, and its analgesic effect lasts 6 to 8 hours. Nevertheless, methadone has been used for a long time for heroin abusers as detoxification and maintenance; it carries a social stigma, which can interfere with adequate pain management. Methadone has an irregular elimination half-life with interindividual variation between 20 and 60 hours. Because of that, the cumulative effect of methadone causes sedation, makes titration difficult, and has led to the concept of individualization of methadone dosing.

Ballantyne JC, Fishman SM, Rathmell JP, et al., eds. *Bonica's Management of Pain*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1682–1710.

Brunton L, Chabner B, Knollman B. *Goodman and Gilman's The Pharmacological Basis of Therapeutics*. 12th ed. New York: McGraw-Hill; 2011:566–578.

B.7. What is the mechanism of action of opioids?

Opioids act as agonists at stereospecific opioid receptors that are normally activated by endogenous ligands known as endorphins in brainstem and spinal cord. Binding of opioid to the receptor inhibits adenylate cyclase activity and causes hyperpolarization of neurons, which results in suppression of spontaneous discharge and evoked potential. Opioids also interfere with transmembrane transport of calcium ion and interfere with the release of neurotransmitters such as acetylcholine, dopamine, norepinephrine, and substance P. Inhibition of acetylcholine release from nerve endings is the basis of analgesic activity of opioids.

Ballantyne JC, Fishman SM, Rathmell JP, et al., eds. *Bonica's Management of Pain*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1682–1710.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:769–825.

B.8. What are the side effects of opioid therapy?

The opioid-related side effects occur because of opioid receptor pharmacodynamics, metabolites, or both. Sedation and respiratory depression are due to μ-receptor

activation. Tolerance to these side effects is developed within a very short period of treatment. The dysphoric reaction is due to activation of κ-receptors. Psychotomimetic and depersonalization reactions are due to activation of σ-receptors. Nausea and vomiting are caused by direct stimulation of the chemoreceptor trigger zone. Increased intrabiliary pressure is due to spasm of the sphincter of Oddi. Other side effects commonly observed are constipation, pruritus, and myoclonus. Almost all side effects diminish with time, except constipation and myoclonus. Patients with cancer who develop constipation secondary to opioid therapy are required to be on a regular bowel regimen to avoid subsequent serious consequences. In patients with compromised renal function, metabolites of morphine (M3G, M6G) cause excessive sedation and metabolites of meperidine (normeperidine) lower the seizure threshold.

Brunton L, Chabner B, Knollman B. *Goodman and Gilman's The Pharmacological Basis of Therapeutics*. 12th ed. New York: McGraw-Hill; 2011:566–578.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:769–825.

B.9. Define tolerance and physical dependence.

Tolerance occurs with the development of the need to gradually escalate the dose to achieve the same pain control, and it can develop in 2 to 3 weeks. Physical dependence develops after chronic use of opioids and it is characterized by development of withdrawal syndrome after administration of an opioid antagonist or abrupt discontinuation of the medication. The potential for tolerance is an agonistic effect of opioids.

Streltzer J, Johansen L. Prescription drug dependence and evolving beliefs about chronic pain management. *Am J Psychiatry*. 2006;163:594–598.

B.10. How would you treat the side effects of opioid therapy?

Oversedation and respiratory depression are treated with a specific μ-receptor antagonist, naloxone, as well as supplemental oxygen. Naloxone, in a 1- to 4-μg per kg intravenous bolus, promptly reverses sedation, respiratory depression, and analgesia. Continuous intravenous infusion at the rate of 2 to 4 μg/kg/hr will reverse only side effects without reversing analgesia. Nausea and vomiting should be managed by antiemetics. Constipation should be treated with a regular bowel regimen of laxatives and stool softener. Methylnaltrexone, a peripheral μ-opioid receptor antagonist with restricted ability to cross the blood–brain barrier, has been shown to improve constipation from opiates without affecting pain relief. Generalized pruritus may respond to one more doses of antihistamine, although pruritus may not be related to histamine release.

Cherny N, Ripamonti C, Pereira J, et al. Strategies to manage the adverse effects of oral morphine: an evidence based report. *J Clin Oncol*. 2001;19:2542–2554.

Slatkin N, Thomas J, Lipman AG, et al. Methylnaltrexone for treatment of opioid-induced constipation in advance illness patients. *J Supp Oncol*. 2009;7:39–46.

B.11. What is tramadol? Is it an opiate? What is tapentadol and how does it compare to traditional opiates?

Tramadol (Ultram) is a nonopioid synthetic analgesic with weak μ-receptor agonistic activity and is thought to exert its analgesic effects by inhibition of reuptake of norepinephrine and serotonin. It should be started at 50 to 100 mg every 6 to

8 hours. It may exhibit μ-receptor–related clinical side effects such as respiratory depression and constipation. Prolonged use may lead to physical and psychological dependence.

Tapentadol is a centrally acting pain reliever, with agonist activity at the μ-receptor, and inhibition of norepinephrine reuptake. Compared to oxycodone IR, tapentadol showed a reduction in gastrointestinal side effects, specifically nausea, constipation, and vomiting. Tapentadol should be administered first in the 50-mg strength and can be increased to 100 mg every 4 to 6 hours as needed. Of note, it too can also cause respiratory depression because it shows μ-opioid agonist activity and is a controlled substance, unlike tramadol.

Both tramadol and tapentadol can cause life-threatening serotonin syndrome with the use of other serotonin–norepinephrine uptake inhibitors, selective serotonin reuptake inhibitors, tricyclic antidepressants, or monoamine oxidase inhibitors and, therefore, should be used with caution in patients on these medications.

Brunton L, Chabner B, Knollman B. *Goodman and Gilman's The Pharmacological Basis of Therapeutics*. 12th ed. New York: McGraw-Hill; 2011:566–578.

Grond S, Sablotzki A. Clinical pharmacology of tramadol. *Clin Pharmacokinet*. 2004;43:879–923.

Hartrick C, Okamoto A, Oh I, et al. Efficacy and tolerability of tapentadol immediate release and oxycodone HCl immediate release in patients awaiting primary joint replacement surgery for end-stage joint disease: a 10-day, phase III, randomized, double-blind, active- and placebo-controlled study. *Clin Therapeut*. 2009;31:260–271.

B.12. When would you consider adjuvant analgesics as part of the treatment plan?

In cancer pain management, adjuvant drugs are considered to enhance pain relief. The adjuvant analgesics are a heterogeneous group of medications originally developed for purposes other than pain relief. These drugs may become necessary in the multimodal approach to treat pain, the adverse effects of analgesic medications, or concomitant psychological disturbances such as insomnia, anxiety, depression, and psychosis. The most useful adjuvants used clinically to manage cancer pain are as follows:

- Corticosteroids
- Tricyclic antidepressants (e.g., amitriptyline)
- Anticonvulsants (e.g., gabapentin)
- Amphetamines
- NMDA receptor antagonists (e.g., methadone, ketamine)
- α_2-Agonists (e.g., clonidine)
- Antihistaminics
- Phenothiazines

Abram S, Haddox J, eds. *The Pain Clinic Manual*. 2nd ed. Philadelphia: Lippincott Williams & Wilkins; 2000:293–351.

Ballantyne JC, Fishman SM, Rathmell JP, et al., eds. *Bonica's Management of Pain*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1682–1710.

B.13. The patient and his family are worried about addiction. How would you approach this problem?

Addiction is defined as a persistent pattern of dysfunctional use of opioids that may involve adverse consequences associated with continued use, loss of control over use of opioids, compulsive use of drug, craving for the drug, and typical drug-seeking

behavior. Patients with chronic pain who are using opioids are not at higher risk for addiction than the general population. The goals of treatment, including palliation of pain and improvement in the patient's quality of life, must be clearly defined and explained to the patient and his relatives. At no time should patients with cancer pain be undertreated because of the fear of addiction. The patient and his family should be educated about the common misconception that addiction is a common outcome of opioid therapy.

Heit HA. Addiction, physical dependence and tolerance: precise definitions to help clinicians evaluate and treat chronic pain patients. *J Pain Palliat Care Pharmacother*. 2003;17:15–29.

B.14. Describe different routes of opioid administration.

Oral medications should be used as the first-line approach in most patients with cancer pain who are receiving opioid analgesics. Table 48.2 outlines the routes of opioid administration and available opioid preparations.

The rectal or transdermal route should be chosen before considering invasive therapy for cancer pain. The sublingual route is limited by the inability to deliver large doses.

The intramuscular route is not preferred for long-term administration because it requires repeated painful injections and offers no pharmacodynamic advantages. Intravenous administration provides quick onset and is ideal for painful crises in patients with cancer as patient-controlled analgesia (PCA).

The equianalgesic doses of opioids used orally and parenterally are listed in Table 48.3.

Table 48.2 Routes of Opioid Administration

ROUTE OF ADMINISTRATION	AVAILABLE OPIOID PREPARATION
Oral	Morphine
	Hydromorphone (Dilaudid)
	Methadone (Dolophine)
	Oxycodone, hydrocodone
	Codeine, meperidine
	Levorphanol
Rectal	Suppositories containing morphine
	Hydromorphone, oxycodone
Transdermal	Fentanyl patch
Sublingual	Fentanyl, methadone, buprenorphine
Intramuscular/subcutaneous	Morphine, hydromorphone, methadone
	Meperidine, levorphanol
Intravenous	Morphine, meperidine, methadone, fentanyl
	Hydromorphone, oxymorphone
Epidural/intrathecal	Morphine, methadone, hydromorphone
	Fentanyl, meperidine

Table 48.3 Opioids Used Orally or Parenterally to Treat Cancer Pain

	EQUIANALGESIC DOSE (mg)[a]	
DRUG	**ORAL**	**PARENTERAL**
Morphine	30	10
Hydromorphone	6	2
Oxycodone	20–30	NA
Methadone	10[b]	10[b]
Levorphanol	2–3[b]	2[b]
Codeine	130[c]	75

[a] Suggested doses are guidelines only. Doses are based on chronic opioid use.
[b] Particular care with titration is recommended, because doses may need to be reduced significantly when steady-state levels are reached after 2 to 3 days.
[c] Codeine doses greater than 65 mg may be associated with significant constipation.
NA, not available in the United States.

Brunton L, Chabner B, Knollman B. *Goodman and Gilman's The Pharmacological Basis of Therapeutics*. 12th ed. New York: McGraw-Hill; 2011:566–578.

Mercadante S. Recent progress in the pharmacology of cancer pain. *Expect Rev Anticancer Ther*. 2001;1:487–494.

B.15. Describe advantages and complications of patient-controlled analgesia (PCA). What is minimum effective analgesic concentration (MEAC)?

Intravenous PCA is very advantageous for patients with chronic cancer pain because it allows patients to self-administer medication and find their own comfort zone between side effects and pain control within limits set by the physician. The PCA device is a computerized, programmable, lightweight, battery-operated portable pump with the capability of storage and retrieval of data by the microprocessor. The pump is programmed for three modes of drug delivery: (1) continuous per-hour rate infusion only, which is preset by the physician and over which the patient has no control; (2) continuous with boluses for breakthrough pain, with boluses controlled by the patient; and (3) boluses with lockout time in minutes set by the physician, with the patient controlling his or her own requirement. If necessary, the physician or nurse can deliver extra boluses. Intermittent rescue doses for breakthrough pain, along with continuous infusion, decrease the total requirement of opioids. The rescue-dose delivery mode is safer because patients will not take medication if there is no pain. Nevertheless, the continuous-delivery mode carries risks of oversedation and respiratory depression. The initial cost of the drug-delivery device and training of the health care provider could be expensive. PCA can also be provided by subcutaneous, epidural, or intrathecal route.

MEAC is the minimum effective analgesic concentration of the opioid that is the lower level of the therapeutic window (Fig. 48.2). The upper level of the therapeutic window represents the serum concentration at which adverse side effects will occur. Neither age, sex, body weight, nor rate of drug elimination appeared to be related to the therapeutic concentration.

Ballantyne JC, Fishman SM, Rathmell JP, et al., eds. *Bonica's Management of Pain*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1682–1710.

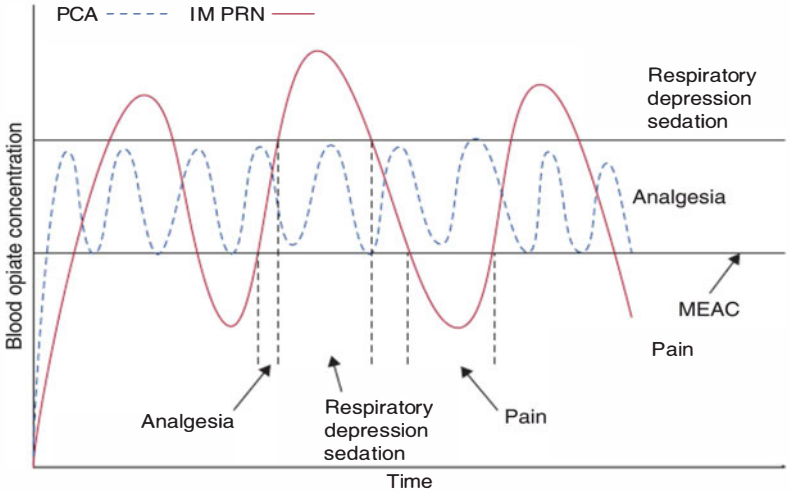


Figure 48.2 The MEAC is the minimum effective analgesic concentration of the opioid that is the lower level of the therapeutic window. IM, intramuscular; MEAC, minimum effective analgesic concentration; PCA, patient-controlled analgesia; PRN, as needed. (Modified from Ashburn M, Smith K. The management of postoperative pain. *Surg Rounds*. 1991;14:129–134.)

B.16. What is meperidine? How is it different from other opioids?

Meperidine is a synthetic opioid that pharmacologically resembles morphine. Meperidine is not an ideal drug for chronic pain because of its short duration of action and its high potential for abuse. The by-product normeperidine is exclusively excreted via the kidney, with an elimination half-life of 36 to 40 hours. In patients with compromised renal function, by-product accumulation has been associated with central nervous system toxicity, including myoclonus, tremulousness, hallucinations, and seizures. Meperidine possesses anticholinergic activity similar to atropine, causing mydriasis, orthostatic hypotension, and tachycardia. Compared with other opioids, meperidine very rarely causes pruritus when given neuraxially. It is extremely effective in the treatment of postoperative shivering. Meperidine also demonstrates local anesthetic actions. It is contraindicated in patients who are receiving monoamine oxidase inhibitors because of the risk of a potentially fatal syndrome characterized by hyperthermia, rigidity, and seizures.

Brunton L, Chabner B, Knollman B. *Goodman and Gilman's The Pharmacological Basis of Therapeutics*. 12th ed. New York: McGraw-Hill; 2011:566–578.

B.17. What is rotation of opioids? When would you consider rotation of opioids?

The sequential trial of changing from one opioid to another when either treatment-limiting toxicity or poor responsiveness develops has become known as *opioid rotation*. The variable response from opioid to opioid in an individual has led to this approach; changing to an alternative opioid may yield a far better balance between side effects and analgesia.

For those patients in whom pain control is inadequate and who have intolerable side effects, different strategies are implemented to improve analgesia. Opioid rotation is a simple strategy that almost all physicians can implement. Depending on equianalgesic potency ratio guidelines, switch is made to other opioids such as methadone or transdermal fentanyl patch. This should be done under close supervision and preferably in an inpatient environment.

Ballantyne JC, Fishman SM, Rathmell JP, et al., eds. *Bonica's Management of Pain*. 4th ed. Philadelphia: Lippincott Williams & Wilkin; 2009:1682–1710.

C. Invasive Therapy

C.1. Describe the role of peripheral nerve blocks in cancer pain management.

The following nerve blocks can be considered depending on the location and distribution of the thoracic or abdominal pain and the involvement of viscera:

- Intercostal nerve blocks
- Interpleural blockade
- Splanchnic nerve blocks
- Celiac plexus block
- Hypogastric plexus block
- Thoracic and lumbar paravertebral somatic nerve blocks
- Rectus abdominis block
- Iliac crest block
- Ilioinguinal and iliohypogastric nerve block
- Cave of Retzius (space between urinary bladder and symphysis pubis) block

Various combinations of peripheral nerve blocks can be performed to aid in the global comfort of the patient by providing better pain control and reducing the total dose of medications and thereby the side effects. The most useful blocks for the upper abdomen and thorax are intercostal nerve blocks and celiac plexus blocks. The splanchnic nerve block and superior hypogastric blocks are the other two that can be considered depending on the location and involvement of the viscera. Thoracic and lumbar paravertebral blocks are performed to obtain spinal nerve segmental analgesia. The intercostal and thoracic paravertebral nerve blocks carry the risk of pneumothorax because of the proximity of the pleura and lung. The peripheral nerve blocks are performed at anatomic sites away from the central neuraxis. More distal blocks have greater chances of incomplete blocks because of spatial distribution, overlap of nerves, and difficulty in blocking multiple branches of arborizing nerve.

DeLeon-Casasola OA. *Pharmacological, Interventional and Palliative Care Approaches*. Philadelphia: Saunders; 2006:531–533.

Waldman SD, ed. *Interventional Pain Management*. 2nd ed. Philadelphia: WB Saunders; 2001:541–553.

C.2. Describe the role of celiac plexus block in cancer pain management.

Diagnostic celiac plexus block with a local anesthetic is performed to precisely differentiate sympathetically maintained pain and localize retroperitoneal or upper abdominal pain. A positive result of the diagnostic block is an indication for more

definitive neurolysis in chronic cancer and nonmalignant pain. Success rates of celiac plexus neurolysis are lower in patients suffering from chronic nonmalignant abdominal pain than in those suffering from abdominal pain of neoplastic origin. Neurolysis of celiac plexus with alcohol or phenol is performed under fluoroscopic guidance or computed tomography–guided technique with strict sterile condition using a single-needle periaortic technique, single-needle transaortic technique, single-needle anterior technique, or endoscopic ultrasound–guided technique. Individual skills of the treating physician, available facilities, patient's general condition, and extent of the spread of tumor should be considered in determining the type of technique to use.

For celiac plexus neurolysis, many pain physicians commonly use 40 to 50 mL of 50% to 70% alcohol or 6% to 10% phenol. Smaller volumes are recommended for absolute alcohol and higher concentration of phenol. Neurolysis with phenol is less painful because of its local anesthetic action, whereas alcohol neurolysis is very painful and should be blocked with pretreatment with local anesthetics.

DeLeon-Casasola OA. *Pharmacological, Interventional and Palliative Care Approaches*. Philadelphia: Saunders; 2006:401–416.

Waldman SD, ed. *Interventional Pain Management*. 2nd ed. Philadelphia: WB Saunders 2001:541–553.

C.3. What are the complications of celiac plexus block?

Serious complications should rarely occur in the hands of a skilled clinician. Hypotension and increased gastrointestinal motility are the most common complications of this block. Neurologic complications include subarachnoid or epidural injection and lumbar nerve root injury, causing long-lasting paresthesia. A potentially severe complication can occur as a result of accidental injection into the nutrient artery of the spinal cord (artery of Adamkiewicz), causing paraplegia. Injury to the kidney may cause temporary hematuria that may not need any treatment. Other complications that have been reported because of the proximity of other vital structures include pneumothorax, chylothorax, intradisc injection, retroperitoneal hematoma, and failure to ejaculate.

Ballantyne JC, Fishman SM, Rathmell JP, et al., eds. *Bonica's Management of Pain*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:605–618.

C.4. Would you consider neuraxial opioid infusion in this patient? Discuss complications of this procedure.

In properly selected patients, epidural, intrathecal (subarachnoid), or intraventricular infusions of opioids have the advantage of producing profound analgesia without motor, sensory, or autonomic blockade. These routes are considered to deliver preservative-free medications when pain is not well controlled by noninvasive (oral, subcutaneous, or intravenous) routes and escalation of doses is limited by intolerable side effects. The potency ratio of oral to epidural morphine is 1:30 and that from oral to intrathecal morphine is 1:300. The decrease in dose size from oral to intrathecal greatly reduces the side effects and improves pain control and quality of life. The PCA technique can also be employed for epidural routes. Programmable intrathecal pumps can deliver medications at the prescribed dose. Fixed or flexible doses of morphine can deliver via the intrathecal pumps.

Stearns L, Boortz-Mark R, Du Pen S, et al. Intrathecal drug delivery for the management of cancer pain. *J Supp Oncol*. 2005;3:399–408.

C.5. Which medications can be used intrathecally? What is ziconotide?

Morphine is the most commonly used drug; other opiates such as hydromorphone and fentanyl can be used intrathecally. In addition, local anesthetics, α-agonists such as clonidine, and baclofen can be used as recommended by the polyanalgesic consensus panel.

Recently, ziconotide (Prialt), a synthetic equivalent of a naturally occurring peptide found in marine snails, has been shown to be effective in pain relief when used intrathecally. It is a selective voltage-gated calcium channel blocker that inhibits release of pro-glutamate, calcitonin, and substance P in the brain and spinal cord. Side effects include dizziness, nausea, confusion, and psychosis and, therefore, patients trialed on ziconotide should be monitored for cognitive impairment, hallucinations, or changes in mood and consciousness.

Stearns L, Boortz-Mark R, Du Pen S, et al. Intrathecal drug delivery for the management of cancer pain. *J Supp Oncol*. 2005;3:399–408.

Williams J, Day M, Heavner J. Ziconotide: an update and review. *Exp Opin Pharmacother*. 2008;9:1575–1583.

C.6. What is a Personal Therapy Manager (PTM) and what role does it play in neuraxial pain relief?

Increasingly being used is a patient-controlled device that allows patient activated doses via the intrathecal pump (Personal Therapy Manager [PTM], Medtronics Neurological, Minneapolis, MN). The PTM enables the patient to activate delivery of physician-programmed supplemental doses of intrathecal medication. This is especially useful for patients experiencing intermittent pain of varying intensity that cannot be adequately managed with a simple continuous infusion, have an unpredictable need for varying doses of drug, or experience inadequate pain relief or intolerable side effects from supplemental systemic breakthrough pain medications. Nevertheless, risk of sedation, respiratory depression, and other adverse effects are just as possible as when taking oral opiate supplementation and, therefore, caution and careful programming should be ensured.

These routes require a skilled experienced clinician, meticulous technique, and family and facility support in which close monitoring and follow-up can be done. These procedures are reversible but involve expenses for specialized care and operating room costs. Intraspinal opioids may produce the same side effects of nausea, mental clouding, and sedation as in oral and parenteral dosing. Infection (e.g., meningitis and epidural abscess) and hematoma are potentially devastating complications that can cause permanent neurologic deficit if not dealt with in a timely basis. Pruritus and urinary retention are more common than with oral or parenteral administration.

DeLeon-Casasola OA. *Pharmacological, Interventional and Palliative Care Approaches*. 1st ed. Philadelphia: Saunders; 2006:417–429.

Rauck, R, Cherry D, Boyer MF, et al. Long-term intrathecal opioid therapy with a patient-activated, implanted delivery system for the treatment of refractory cancer pain. *J Pain*. 2003;4:441–447.

Stearns L, Boortz-Mark R, Du Pen S, et al. Intrathecal drug delivery for the management of cancer pain. *J Supp Oncol*. 2005;3:399–408.

C.7. Would you consider neuraxial neurolysis in this patient to manage his pain? Discuss advantages and disadvantages of these blocks.

Because of the physical separation of motor and sensory nerve roots in the spinal canal and intrathecal space, chemical neurolytic procedures allow sensory blockade without loss of motor functions. Inadequate pain control with intolerable side effects makes this patient an ideal candidate for neuraxial neurolysis; nevertheless, complications of the procedure should be weighed against benefits. Epidural or intrathecal (subarachnoid) neurolytic blocks are considered for severe intractable pain from advanced cancer as an adjuvant to relieve pain and suffering and improve quality of life. These blocks are primarily effective in relieving pain of somatic origin and less effective for visceral and neuropathic pain.

In selected patients in whom pain relief is not achieved by less invasive measures, these blocks can provide rapid analgesia and allow dosage (and side effects) reduction of systemic drugs. Nevertheless, the risks of postural hypotension, bowel and bladder incontinence, and motor and sensory deficit in the lower extremities cannot be overemphasized. These blocks are irreversible and require a skilled clinician to perform the procedure.

DeLeon-Casasola OA. *Pharmacological, Interventional and Palliative Care Approaches*. 1st ed. Philadelphia: Saunders; 2006:501–507.

C.8. Which neuroablative procedures can be considered in the terminal stage of pancreatic cancer?

Based on the location and type of pain (somatic, visceral, deafferentation), the general condition of the patient, the stage of tumor and metastasis, the life expectancy, and the expertise available, the following neurosurgical procedures could be considered:

- Peripheral neurectomy
- Dorsal rhizotomy
- Anterolateral cordotomy (spinal tractotomy)
- Commissural myelotomy
- Hypophysectomy

Ballantyne JC, Fishman SM, Rathmell JP, et al., eds. *Bonica's Management of Pain*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:605–618.

C.9. Describe the role of radiation therapy in cancer pain.

Radiation therapy can relieve pain from metastasis and symptoms from local extension of the disease. Radiation therapy is palliative and complementary to analgesic drug therapies to enhance the effectiveness of pain control. Along with therapeutic effectiveness of radiation treatment, the absence of complete specificity for disease may exacerbate or even cause new pain. The radiation dosage should be administered in the fewest fractions possible to promote pain control during and after treatment.

Benzon H, Rathmell J, eds. *Raj's Practical Management of Pain*. 4th ed. St. Louis, MO: Mosby; 2008:418–426.

McQuay HJ, Collins SL, Carroll D, et al. Radiotherapy for the palliation of painful bone metastases. *Cochrane Database Syst Rev*. 2000(2):CD001793.

D. Nonpharmacologic Management

D.1. What are the various nonpharmacologic techniques of cancer pain management?

Eisenberg et al. demonstrated that cancer and other chronic pain syndromes such as AIDS and arthritis may receive benefit from alternative modalities. The common therapies offered are as follows:

- Physical therapy and physical modalities
- Relaxation and massage
- Chiropractic manipulation
- Spiritual healing
- Biofeedback and hypnosis
- Magnetic and low-power laser therapy
- Transcutaneous electrical nerve stimulation
- Homeopathy
- Acupuncture
- Prayer

Benzon H, Rathmell J, eds. *Raj's Practical Management of Pain.* 4th ed. St. Louis: Mosby; 2008:418–426.

Bradley L, McKendree-Smith N, Cianfrini L. Cognitive-behavioral therapy interventions for pain associated with chronic illness: evidence for their effectiveness. *Semin Pain Med.* 2003;1:44–54.

D.2. What physical modalities have been successfully tried in cancer pain management?

Physical modalities may help decrease stiffness, increase blood flow to the part, help relax the patient, and reduce the dose of analgesics. They include cutaneous stimulation, superficial heat and cold therapy, massage, vibration, and pressure. Cold therapy (cryotherapy) causes vasoconstriction, reduces inflammation, and decreases muscle spasm. Superficial application of heat (thermotherapy) acts through conduction or convection to increase blood flow to the skin and superficial organs. Heat also decreases joint stiffness and increases muscle flexibility. Physical therapy and exercise help to strengthen weak muscles, mobilize stiff joints, and restore coordination. Exercise may reduce pain by 25%. Weight-bearing exercises are avoided if an impending fracture is suspected.

Benzon H, Rathmell J, eds. *Raj's Practical Management of Pain.* 4th ed. St. Louis: Mosby; 2008:418–426.

Santiago-Palma J, Payne R. Palliative care and rehabilitation. *Cancer.* 1999;92:1049–1052.

D.3. Describe the role of neuromodulation in cancer pain management.

Neuromodulation techniques such as spinal cord stimulation and deep brain stimulation have not been popular in cancer pain management. Neuromodulation techniques have variable outcome results with success rates between 18% and 80% depending on the study cited. Much of the literature is about chronic nonmalignant pain syndromes. The consensus among most pain physicians is that neuropathic pain syndromes are more effectively treated as spinal cord syndromes than as nociceptive pain syndromes. Thus, spinal cord stimulation and deep brain stimulation should offer relief of neuropathic pain syndromes in patients with cancer.

Transcutaneous electrical nerve stimulation and acupuncture are believed to activate endogenous pain-relieving pathways. Low-voltage stimulation to large myelinated peripheral nerves via cutaneous electrodes may significantly reduce pain.

Acupuncture is a neuromodulatory technique that treats pain with insertion of needles in skin and underlying muscles. Based on various Chinese scientific principles, acupuncture is becoming very popular in Western medical systems. Many intrinsic factors contribute to the success of acupuncture, and in selected patients it does control pain.

Nguyen JP, Lefaucher JP, Le Guerinel C, et al. Motor cortex stimulation in the treatment of central and neuropathic pain. *Arch Med Res.* 2000;31:263–265.

Oakley JC, Prager JP. Spinal cord stimulation: mechanism of action. *Spine.* 2002;27: 2574–2583.

Yakovlev A, Ellias Y. Spinal cord stimulation as a treatment option for intractable neuropathic cancer pain. *Clin Med Res.* 2008;6:103–106.

D.4. What psychological techniques have been promoted for comfort care and pain relief?

Psychological interventions are an important part of a multimodal approach to pain management in patients with cancer. It helps patients gain a sense of control over pain. Cognitive and behavioral techniques are designed to influence the interpretation of events and bodily sensations. Cognitive techniques help patients think differently about their pain and its management. Behavioral techniques help patients develop skills to cope with pain and help modify their reactions to pain. Patients who undergo psychotherapy report less pain. Relaxation therapy is a well-established modality in managing cancer pain. Several variations of relaxation strategies and techniques have been widely practiced in patients suffering from advanced cancer and have proven effective. Relaxation strategies such as deep breathing, muscle relaxation, and imagery are recommended for the promotion of comfort and relief of pain in hospitalized patients.

Relaxation and imagery are used to achieve a state of mental and physical relaxation, thereby relieving anxiety and muscle tension.

NIH Consensus Conference State of the Science Conference Statement on Symptom Management in Cancer. *Pain, Depression and Fatigue.* Bethesda, MD: National Institute of Health; 2002.

D.5. What are distraction and reframing techniques? What is the role of hypnosis in cancer pain management?

Distraction and reframing techniques encourage focused attention on stimuli other than pain. This involves singing, talking, praying, and watching television. Reframing helps monitor and evaluate negative thoughts and images while encouraging positive thoughts and behavior.

Hypnosis by a skilled person decreases pain and anxiety in patients who have difficulty managing their pain. It also increases coping skills. This technique allows heightened awareness and focused concentration to manipulate perception of pain and has been effective in the management of cancer-related pain syndromes.

Benzon H, Rathmell J, eds. *Raj's Practical Management of Pain*. 4th ed. St. Louis: Mosby; 2008:418–426.

Devine EC. Meta-analysis of the effect of psychoeducational interventions on pain in adults with cancer. *Oncol Nurs Forum.* 2003;30:75–89.

CHAPTER 49

Low Back Pain and Sciatica

DAVID Y. WANG AND JEFFREY Y. F. NGEOW

A 57-YEAR-OLD FORMER FACTORY WORKER was injured on the job 8 years ago. He experienced severe low back and right leg pain after lifting a heavy piece of equipment and was found to have a herniated L4-5 intervertebral disc with compression of the right L5 nerve root. He underwent a laminectomy and decompression; nevertheless, he has continued to complain of back pain.

A. Medical Disease and Differential Diagnosis

1. How great an issue is low back pain in the general population?
2. What is the prevalence of low back pain?
3. What is the societal cost of low back pain?
4. What are the risk factors for low back pain?
5. What are the potential sources of pain in the spine?
6. What is the anatomy of the intervertebral discs? What is the mechanism of pain from herniated discs?
7. What is the anatomy of the spinal facets? How do the facet joints cause pain?
8. What are the important findings in the history and physical examination?
9. Which are the appropriate diagnostic studies for low back pain?
10. What is the differential diagnosis of low back pain?
11. What are the causes of multiple spine surgeries and persistent back pain?

B. Management of Low Back Pain and Sciatica

1. What are the noninterventional treatments available?
2. What are the traditional interventional treatments available and how should they be used?
3. What are some of the recent advances in minimally invasive interventions?
4. When should surgery be considered?
5. What new surgical options are now available for treatment of disc disease?

A. Medical Disease and Differential Diagnosis

A.1. How great an issue is low back pain in the general population?

Disorders of the lumbosacral spine cause pain, disability, suffering, public health issues, and socioeconomic issues with far greater impact than disorders of any other part of the body. Most adults will experience several episodes of low back pain during their lifetime. It is estimated that 80% of workers will lose work time because of this complaint. On the basis of primary diagnosis only, a National Ambulatory Medical Care Survey in 1989 to 1990, ranked low back pain as the fifth most frequent reason for adults to visit an office-based medical practice. In surveys employing a wider definition of low back pain, it was found to be the second most frequent symptom prompting physician office visits in the United States.

Hart LG, Deyo RA, Cherkin DC. Physician office visits for low back pain: frequency, clinical evaluation, and treatment patterns from a U.S. national survey. *Spine.* 1995;20:11–19.

Manchikanti L. Epidemiology of low back pain. *Pain Physician.* 2000;3:167–192.

A.2. What is the prevalence of low back pain?

Low back pain usually begins in early life, with the highest frequency of symptoms occurring between ages 35 and 55. Of all adults in industrialized societies, 60% to 80% are affected at some point in their lives. Work absence and symptom duration increase with aging. An acute episode of low back pain usually resolves within 6 weeks. Up to 50% of all adults report having an episode of low back pain during a given year, and approximately 15% of these patients complain of frequent low back pain or pain lasting longer than 2 weeks during a given year. More persistent pain lasting beyond 3 to 6 months occurred in only 5% to 10% of patients with back pain. The U.S. Agency for Health Care Policy and Research reported that 90% of patients with acute low back pain recover their usual activity tolerance within 4 weeks of injury. The remaining 10% of patients who do not recover with time or routine therapy go on to develop chronic symptoms and secondary problems. Using data from the National Health and Nutrition Examinations Survey II, Deyo et al. reported that 1.6% of adults reported symptoms of both back pain and sciatica (lasting for at least 2 weeks). Only 2.1% of respondents had ever been told they had a "ruptured disc" in the lower back. In other clinical studies, it was estimated that as few as 1% to 30% of low back pain can be attributed to nerve root compression. According to the 14-year interval study in North Carolina, the prevalence of chronic, impairing low back pain rose significantly over the 14-year interval, from 3.9% in 1992 to 10.2% in 2006. Recurrences of low back pain are also common, with the percentage of subsequent low back pain episodes ranging from 20% to 44% within 1 year for working populations to lifetime recurrences of up to 85%.

Deyo RA, Tsui-Wu YJ. Descriptive epidemiology of low back pain and its related medical care in the United States. *Spine.* 1987;12:264–268.

Fordyce WE, ed. Back pain in the workplace. In: *Task Force on Pain in the Workplace: Management of Disability in Nonspecific Condition*. Seattle: IASP Press; 1995:43–56.

Freburger JK, Holmes GM, Agans RP, et al. The rising prevalence of chronic low back pain. *Arch Intern Med.* 2009;169:251–258.

Loney PL, Stratford PW. The prevalence of low back pain in adults: a methodological review of the literature. *Phys Ther.* 1999;79:384–396.

Manchikanti L. Epidemiology of low back pain. *Pain Phys.* 2000;3:167–192.

Rubin DI. Epidemiology and risk factors for spine pain. *Neurol Clin.* 2007;25:353–371.

A.3. What is the societal cost of low back pain?

The cost to society of low back pain is enormous. Robertson et al. indicate that the prevalence of back symptoms and objective impairment to function have been unchanged over the last several decades. It appears that the societal perception of disability has changed dramatically over the same period. This has resulted in an increased rate and cost of disability and overutilization of medical care, including surgical treatments. In 1992, the estimates of costs, morbidity, and mortality of occupational injury or illness in the United States were $171 billion, counting direct costs of $65 billion and indirect costs of $106 billion. Injuries accounted for $145 billion spent and illness $26 billion. It is estimated that 75% or more of these costs can be attributed to the 5% of people who become disabled temporarily or permanently from back pain. Occupational low back pain accounts for at least 33% of all healthcare and indemnity costs under workers' compensation. These numbers have been confirmed by recent research supported by the National Institute of Arthritis and Musculoskeletal and Skin Disease.

Katz JN. Lumbar disc disorders and low-back pain: socioeconomic factors and consequences. *J Bone Joint Surg Am.* 2006;88:21–24.

Leigh JP, Markowitz SB, Fahs M, et al. Occupational injury and illness in the United States: estimates of costs, morbidity, and mortality. *Arch Int Med.* 1997;157:1557–1568.

Robertson JT. The rape of the spine. *Surg Neurol.* 1993;39:5–12.

Volinn E, Turczyn K, Loeser JD. Theories of back pain and health care utilization. *Neurosurg Clin North Am.* 1991;2:739–748.

Williams DA, Feuerstein M, Durbin D, et al. Health care and indemnity costs across the natural history of disability in occupational low back pain. *Spine.* 1998;23:2329–2336.

A.4. What are the risk factors for low back pain?

Traditional beliefs suggested that heavy physical jobs required high energy demand and significant stress and strain on the spine, whereas light jobs required low energy demand. Many low-energy jobs, nevertheless, are static, which is an inherent risk factor for low back pain. Low back pain, degenerative disc disease, and disc herniation are associated with the following:

- Repetitive heavy lifting
- Static work posture (sitting or standing)
- Frequent twisting and bending
- Vibration (operation of motor vehicle or industrial device)
- The common vibration of construction vehicles and industrial devices ranges in frequency from 3.5 to 8.9 Hz.
- Low-frequency vibration, especially around 5 Hz, in conjunction with a prolonged seated position is associated with spine problems.
- The potential for damage to the disc through mechanical resonance is analogous to the high notes of an operatic soprano shattering wine glasses.
- Fatigue of the abdominal and paraspinal muscles has been demonstrated when subjected to 30 minutes of vibration. In the absence of this support, the spine is further susceptible to injury.
- A meta-analysis of 17 studies revealed that whole-body vibration is associated with an increased risk of low back pain, sciatica, and lumbar intervertebral disc disorders.
- Cigarette smoking. Smoking is linked to low back pain, sciatica, and lumbar disc herniation.
  - In an animal model, cigarette smoking significantly affects the vasculature outside the intervertebral disc, where the most pronounced effect is the reduction of solute-exchange capacity, cellular uptake, and metabolism within the disc.

- Cross-country skiing. In a study of skiing and spinal trauma, the diagonal body position required for cross-country skiing was the most common back pain–inducing stance, whereas no skier experienced back pain when only downhill skiing.

The "oxidative stress hypothesis of aging" theory proposed that enhancement of oxygen consumption resulting from increased physical activity may accelerate disc degeneration. On the other hand, strenuous exercises may contribute to positive nutritional effect by facilitating the transport of small solutes into and out of the disc. Generally, it is believed that persons who are physically fit or who maintain a balanced exercise program appear to have a lower risk for chronic low back pain and a more rapid recovery after an episode of acute back pain.

Biering-Sqrensen F, Thosen C. Medical social and occupational history as risk indicators for low-back trouble in a general population. *Spine.* 1986;11:720–725.

Bovenzi M, Hulshof CT. An updated review of epidemiologic studies on the relationship between exposure to whole-body vibration and low back pain (1986–1997). *Int Arch Occup Environ Health.* 1999;72:351–365.

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Frymoyer JW, Pope MH, Clements JH, et al. Risk factors in low back pain. *J Bone Joint Surg Am.* 1983;65:213–218.

Frymoyer JW, Pope MH, Kristiansen T. Skiing and spinal trauma. *Clin Sports Med.* 1982;1:309–318.

Holm A, Nachemson A. Nutrition of the intervertebral disc: acute effects of cigarette smoking—an experimental animal study. *Ups J Med Sci.* 1988;93:91–99.

Jerkins RR, Goldfarb A. Introduction: oxidant stress, aging, and exercise. *Med Sci Sports Exerc.* 1993;25:210–212.

Porter RW. Does hard work prevent disc protrusion? *Clin Biomech.* 1987;2:196–198.

Sohal RS, Allen RG. Oxidative stress as a causal factor in differentiation and aging: a unifying hypothesis. *Exp Gerontol.* 1990;25:499–522.

Wilder DG, Woodworth BB, Frymoyer JW, et al. Vibration and the human spine. *Spine.* 1982;7:243–254.

A.5. What are the potential sources of pain in the spine?

In order to more easily identify the various sources of pain, the spine may be divided into three compartments: anterior, middle, and posterior.

The anterior compartment consists of the vertebral body and intervertebral disc. The anterior unit is bound together by cephalocaudal ligaments: anterior longitudinal ligament and posterior longitudinal ligament (PLL). The anterior longitudinal ligament is anatomically much broader and stronger than the PLL. The PLL is intact throughout the length of the vertebral column until it reaches the lumbar vertebrae. From L1, it becomes progressively narrower until at L5-S1 it is only half of its original width. This anatomic feature contributes to an inherent structural weakness in the lumbar spine. Hence, the lower lumbar spine is the region subjected to the greatest static stress and most spinal movement resulting in the greatest kinetic strain.

The middle (neuraxial) compartment contains all of the structures within the bony and ligamentous boundaries of the spinal canal. This includes the PLL, epidural space, meninges, spinal cord, dorsal and ventral nerve roots, root sleeves, dorsal root ganglia, and ligamentum flavum.

The posterior compartment contains the facet joints, laminae, vertebral arches, and structures posterior to the plane of the transverse processes and innervated by the dorsal rami of the spinal nerves. The ligaments are extremely important in stabilizing the vertebral column. The ligamentum flavum (yellow ligament), which connects the

laminae of adjacent vertebrae, is the thickest and strongest ligament in the lumbar region. It can contribute to spinal stenosis by folding inward during upright posture, extension of the back, and hypertrophy.

The sinovertebral nerve originates lateral to the neural foramina and enters the spinal canal anterior to the dorsal root ganglion. It is a branch of the somatic ventral nerve root and the sympathetic grey ramus communicans. This specific nerve, also known as the nerve of Luschka, innervates the outer annulus of the disc, PLL, epidural membranes, and dura at the segmental level of origin and adjacent levels. It is important to note that central low back pain, with or without referred pain to the buttocks, may derive from irritation of the outer part of the annulus fibrosis or the PLL.

In summary, the potential sources of low back and radicular pain include the bony structure of vertebrae, muscles attached to the spine and hips, fasciae, ligaments, discs, facet joints, meninges, vessels, nerve roots, dorsal root ganglia, and nerves in the surrounding areas.

The natural wear and tear on the discs and facet joints results in microtrauma and degeneration. This can induce the release of neurohumoral mediators such as phospholipase A_2, serotonin, H^+, substance P, prostaglandin E_2, and so on, to produce inflammation of the nerve roots or meninges, and sensitize local nociceptors. Furthermore, it has been theorized that material from the nucleus pulposus, sheltered from the immune system by the presence of the annulus fibrosis, might act as a foreign protein and trigger an autoimmune reaction. The recent demonstration of an activated immunocompetent cellular response at the epidural interface of the herniation of the nucleus pulposus supports the concept of the immunogenic capacity of the nucleus pulposus. Tissue injury or inflammation can cause a barrage of nociceptive input into the spinal cord. This may lead to a phenomenon called *central sensitization* or *wind-up* of neurons in the dorsal horn of the spinal cord. The release of excitatory amino acids and neuropeptides in the dorsal horn is thought to be the mechanism underlying the phenomenon of central sensitization. At the cellular level, there is an increase in spontaneous discharge and an expansion of neural receptive fields of wide-dynamic-range neurons located in Rexed lamina V of the spinal cord. Clinically, this is characterized by sensation of pain when exposed to nonnoxious stimuli (allodynia), significantly increased response to painful input (hyperalgesia), and increased response to repetitive stimulation (hyperpathia).

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Cavanaugh JM. Neural mechanisms of lumbar pain. *Spine*. 1995;20:1804–1809.

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Manchikanti L. Transforaminal lumbar epidural steroid injection. *Pain Physician*. 2000; 3:374–398.

Olmarker K, Rydevik B. Pathophysiology of sciatica. *Orthop Clin North Am*. 1991;22: 223–233.

Olmarker K, Rydevik B, Nordborg C. Autologous nucleus pulposus induces neurophysiologic and histologic changes in porcine cauda equina nerve roots. *Spine*. 1993;18:1425–1432.

Saal JS. The role of inflammation in lumbar pain. *Spine*. 1995;20:1821–1827.

Williams GW. Low back pain: cost-effective diagnosis and treatment. *Contemp Int Med*. 1995;7:27–42.

A.6. What is the anatomy of the intervertebral discs? What is the mechanism of pain from herniated discs?

The intervertebral disc is a ring-like structure composed of a centrally located well-hydrated pliable proteoglycan matrix, the nucleus pulposus, which comprises two-thirds of the surface area of the disc. Surrounding the nucleus is a fibrocartilaginous ring composed predominantly of type I collagen, the annulus fibrosus, which makes up the remaining one-third of the surface area of the disc. The annulus fibrosus is stronger anteriorly but often defective posteriorly. As a self-contained fluid system, the disc absorbs shock, permits transient compression, and allows movement. It provides a cushion between the vertebral bodies and allows for greater flexibility.

As the disc ages, the number of viable cells in the nucleus pulposus decreases, and the proportion of cells that exhibit necrosis changes from 2% in infancy to 50% in young adults and 80% in the elderly. The water content in the young disc is 80% to 90% in the nucleus pulposus. With aging, the discs tend to dehydrate, losing up to 70% of their water content. As the nucleus pulposus further dehydrates, it becomes more fibrous and less compliant. A disc will usually herniate under strain and pressure. When overstressed, it will protrude along in the path of least resistance, usually posterolaterally. This can cause direct mechanical pressure on the nerve roots resulting in radiculopathy.

In the healthy back, only the outer third of the annulus fibrosus is innervated. In the degenerative or disrupted disc, small unmyelinated nerve fibers grow into the inner third of the annulus fibrosus and even into the nucleus pulposus. Internal disc disruption is a condition characterized by a degenerated nucleus pulposus with radial fissures extending into the peripheral annulus fibrosus. Upon rupture of the disc, the release of irritative material near the meninges can induce radiculitis and symptoms of radiculopathy without actual herniated disc material compressing the nerve roots. Under such circumstances, significant disc herniation might not be visualized on magnetic resonance imaging (MRI) or computed tomography (CT) scan. In brief, the proposed mechanisms of radiculopathy include direct pressure on nerve fibers as a result of compression injury and indirect impact through impairment of microcirculation, chemical irritation and inflammation, immune reaction, edema formation secondary to permeability changes of the intraneural capillaries, and impairment of the nutritional transport to the nerve root.

Compression of the nerve roots is dependent upon the effective space available within the neural foramina, the osseous structures surrounding the neural foramina, and the tethering effects of the intraspinal and extraspinal ligaments. Posterolateral disc herniations can impinge on the lumbar dorsal root, which then initiates electrical discharges for as long as 25 minutes after the mechanical stimulus has been removed. Radiculopathy can be produced by either biochemical or mechanic stimulation of a swollen, stretched, or compressed nerve root. Approximately 3% to 12% of all lumbar disc herniations occur laterally and extend into or beyond the foraminal zone; in this setting, the patients will complain of sudden and severe radicular pain, often with dysesthesia. On the other hand, discogenic pain resulting from a central disc bulge or herniation stimulates several lumbar tissues such as the outer layer of the annulus fibrosus or PLL. Clinically, this is manifested as central low back pain without any radicular symptoms.

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A.7. What is the anatomy of the spinal facets? How do the facet joints cause pain?

The facet, or zygapophysial, joints consist of two arthrodial joints superiorly and inferiorly, each lined with synovium, lubricated by synovial fluid, contained within a joint capsule. These synovial joints enhance spinal stability and flexibility. In the upper part of the lumbar spine (L1–3), the facet planes lie in a generally vertical sagittal plane and permit flexion and extension but prevent lateral flexion or bending in the lordotic curve. The lumbosacral facet joints at the level of L5-S1 depart the farthest from the sagittal plane, allowing some rotation of the lower part of the lumbar spine. With slight forward flexion, the facets of the other lumbar vertebrae separate and permit a modest degree of lateral movement and rotation. Facet loading, if of a repetitive nature, may play a role in the degeneration of the facet joint. After repeated wear and tear, these joints are susceptible to osteoarthritis and associated synovial cyst formation. Hypertrophic facet joints or cysts can encroach on the spinal canal or the intervertebral foramina and contribute to the development of central spinal or foraminal stenosis.

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A.8. What are the important findings in the history and physical examination?

A problem-focused pain history should include onset, location, intensity (e.g., pain scale 0 to 10), characteristics (achy, spasmodic, stabbing, burning, shooting, etc.), duration plus aggravating and alleviating factors. The essential purpose in the initial evaluation is to differentiate patients with serious underlying pathology from those with mild problems.

Patients with a disc problem will usually experience an exacerbation of their symptoms with spinal flexion, which increases intradisc pressure. By contrast, in the setting of spinal stenosis, standing or walking exacerbates back and leg pain, whereas forward flexion may alleviate these symptoms. In moderate-to-severe spinal stenosis, extension of the spine may cause radicular pain.

Patients with compression fractures typically present with severe back pain, often intense with minimal lateral rotation or with flexion and relieved by rest. A history of bladder, bowel, or sexual dysfunction may indicate compression of the cauda equina or conus medullaris. Unlike sciatica, often with its unilateral nerve root involvement, patients with cauda equina syndrome usually have bilateral involvement. Although motor function may be normal and pain uncommon in those with conus lesions, patients often demonstrate abnormalities of sensation in a saddle distribution, feeling touch or dysesthesias but neither pain nor temperature. Causes of these symptoms may be a fracture of L1 or L2, tumor, large central disc herniations, or intramedullary cysts affecting the conus. These disorders are considered surgical emergencies and require aggressive evaluation and prompt surgical consultation.

The physical examination should include Lasègue's sign (the straight leg raising test), Braggard's test (dorsiflexion of the ankle with elevation of the leg), and the crossover test. These clinical tests are considered positive when sciatica is reproduced with elevation of the leg between 30 and 60 degrees. If testing the uninvolved leg produces contralateral symptoms, disc disease should be considered. A positive crossover sign occurs when straight leg raising of the patient's contralateral leg elicits pain on the affected side. It is usually a strong indication of nerve root irritation or compression. Extension of the knee while in a seated position, also known as *distracted straight leg raise*, can test sciatic nerve tension too. The patient with significant nerve root irritation tends to complain of increased pain or lean backward to reduce tension on the nerve. The differential diagnosis of spinal shock, upper motor neuron lesions, and lower neuron lesions is shown in Table 49.1. The nerve root signs are shown in Table 49.2.

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Table 49.1 Differentiating Spinal Shock, Upper Motor Neuron Lesions, and Lower Motor Neuron Lesions

DISEASE STATE	DEEP TENDON REFLEX	PATHOLOGIC REFLEX/ PLANTAR RESPONSE	SUPERFICIAL REFLEX (NORMAL)
Spinal shock	Absent	Absent	Absent
Upper motor neuron disease	Increased; rarely may be decreased in the acute setting	Positive/extensor Babinski's sign + Oppenheim's sign +	Decreased or absent e.g., Cremasteric reflex −
Lower motor neuron disease	Decreased	Negative/flexor	Present (but L1 L2 lesion will have Cremasteric reflex −)

Table 49.2 Nerve Root Signs

ROOT LEVEL	REFLEX DECREASE	SENSORY DEFECT	MOTOR WEAKNESS
L4	Knee jerk	Anterior thigh, knee, and shin	"Single squat and rise test"; quadriceps (mostly L4)
L5	No easily elicited reflex	Lateral leg and middle dorsal foot	"Heel walk test"; dorsiflexion of foot and toes (L5 and some L4); especially big toe, extensor hallucis longus (EHL)
S1	Ankle jerk	Posterior calf and sole	"Toe walk test"; gastrocnemius/soleus; "toe flexors"

A.9. Which are the appropriate diagnostic studies for low back pain?

In the absence of signs of serious medical disease, there is no need for special studies, because 90% of patients will recover spontaneously within 4 weeks of the onset of pain. Waiting 4 weeks before considering special tests allows these patients to recover spontaneously and avoid unneeded procedures. When pain persists beyond 4 to 6 weeks, plain radiographs of the spine should be considered. Pertinent findings include the height of the intervertebral spaces and vertebral bodies, and bony changes in the endplates. With oblique views, the facet joint space and any spondylolysis can be revealed. The lateral view can help estimate the severity of spondylolisthesis. A CT scan can show a herniated disc or fragment in the spinal canal. It can help to identify early epidural hematoma. With contrast, it can help further differentiate tumors, abscesses, and granuloma in the central nervous system. MRI provides excellent anatomic definition of the disc and its hydration status; it can also show the anatomy of the surrounding soft tissues. MRI with intravenous gadolinium is indicated for distinguishing between a recurrent disc herniation and recent postoperative scar tissue. It is particularly useful when distinguishing intrinsic from extramedullary or epidural spinal cord lesions. When MRI is contraindicated, a myelogram may reveal a filling defect at the level of posterior bulging discs. The myelogram in conjunction with a CT scan enables axial imaging of the spinal cord and subarachnoid space. A bone scan is helpful in the diagnosis of bone or bony fractures that may not be visible by radiography or CT scan, or whenever metastatic disease is suspected.

Discography/discogram/discomanometry (discometry) is a specialized diagnostic test specifically indicated to help diagnose discogenic pain. The presence of pain fibers in the outer third of the annulus fibrosus may explain back pain in some individuals with an annulus tear or internal disc disruption. The test involves an intradiscal puncture and instillation of contrast into the disc nucleus. It provides direct confirmation of nuclear morphology and integrity of the vertebral endplate and annulus.

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A.10. What is the differential diagnosis of low back pain?

There are numerous diagnostic labels used to describe low back pain, for example, lumbosacral sprain, lumbar discogenic syndrome, mechanical low back pain, spinal stenosis, spondylosis, spondylolisthesis, osteoarthritis/facet joint syndrome, myofascial pain syndrome, unstable low back, discitis, and failed back surgery syndrome. Each of these labels suggests its own underlying pathology. Acute lumbosacral sprain, by far the most common cause of new-onset low back pain, is often only associated with the presence of postural back pain. It frequently results from reflex muscle spasm secondary to local irritation of structures in the back. When muscle spasm occurs, the normal anatomy may be disturbed and undue force applied to surrounding tissues and structures. In every case, a careful history, physical examination, and the appropriate diagnostic studies will help elucidate the "pain generator."

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A.11. What are the causes of multiple spine surgeries and persistent back pain?

Persistent back or leg pain after one or more spinal surgeries is called *failed back surgery syndrome* or *postlaminectomy syndrome*. Usually, the cause is a combination of both nociceptive and neuropathic pain. Over time, a strong psychological component can develop with progressive disability as treatments fail. Approximately 37,500 patients are diagnosed with this syndrome annually in the United States.

When pain persists or recurs in a patient after spinal surgery, the most common neuroradiologic finding is usually that of epidural fibrosis and scarring besides recurrent disc herniations and spinal stenosis. Patients with this condition often report constant dull, aching, poorly localized low back pain with intermittent sharp episodes. They may also report pain or abnormal sensations with neuropathic characteristics such as burning, shooting, throbbing, stabbing, or pulling. The exact source of these complaints is unclear although the scar tissue or arachnoiditis is frequently implicated. When reoperation is performed for the purpose of neurolysis only, a transient improvement of sciatica may be seen, but it usually recurs within the first postoperative year. Success rates for reoperating on patients with failed back surgery syndrome have been highly variable, ranging from 25% to 80%. These patients are perhaps the most challenging of all. They deserve a comprehensive multidisciplinary evaluation, including orthopedic and neurosurgical consultations. Further, surgical intervention should be avoided in the absence of a clear indication.

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B. Management of Low Back Pain and Sciatica

B.1. What are the noninterventional treatments available?

The cornerstone of treatment for low back pain and mild sciatica caused by a herniated lumbar disc is conservative care, which includes bed rest, medications, and physical therapy. Patients whose symptoms fail to respond to conservative care may require more invasive treatment.

Both clinical and epidemiologic evidence suggests that the longer the back pain and work loss persist, the less likely there will be improvement of the pain. The chance for return to work is even lower. Improved early management and greater access to primary care services should greatly reduce the number of patients with simple backache who require referral to hospitals. Over the last decades, there has been a paradigm shift in the treatment of low back pain away from focusing care exclusively on the pain in favor of helping patients improve their activity tolerance and function. An early return to activity seems to be associated with a better outcome than does prolonged bed rest (greater than 4 days).

Treatment varies depending on the cause of pain. In December 1994, the Agency for Health Care Policy and Research announced the following guidelines for the care of acute low back problems.

- A brief period of rest
- Over-the-counter pain relievers
- Trunk-strengthening exercises
- A single spinal manipulation

In order to avoid reinjury, an incremental, gradually increasing regimen of aerobic exercise (up to 30 minutes daily) can usually be started within the first 2 weeks of symptom onset. Such activities have been found to stress the back no more than sitting for an equal period on the side of the bed. The combination of aerobics for general fitness with some specific training to improve the strength and endurance of the back muscles is often beneficial.

The role of medications in the treatment of low back pain is to control pain, facilitate rehabilitation, restore normal sleep patterns, and improve mood and motivation. Nonsteroidal anti-inflammatory drugs are an essential part of the treatment of patients with inflammatory back pain, such as that associated with spondylitis. Other medications that have been shown to be useful include tricyclic antidepressants and anticonvulsants. Muscle relaxants are often used to decrease muscle spasm and assist in promoting rest for patients with severe pain. These are usually indicated for short-term treatment and acute relief. Short-term therapy with opioid analgesics may be needed to promote rest as well as maintain activity in the acute phase of low back pain. Long-term use of these medications is generally discouraged, but may be appropriate for carefully selected patients.

When recovery does not occur within 6 weeks and no additional pathology is detected, physical therapy is indicated. Patients should be encouraged to increase activity. Activities and postures that increase stress on the back also tend to aggravate back symptoms. Patients limited by back symptoms can minimize the stress of lifting by keeping any lifted object close to the body at the level of the navel. Activities such as twisting, bending, and reaching while lifting, also increase stress on the back. Prolonged sitting may aggravate back symptoms in discogenic pain patients because of progressive increase in pressure at specific points in the abnormal disc. Body weight optimization and a program that teaches good posture and body mechanics are also important. Neuromuscular reconditioning must be included to ensure a function-specific, task-oriented program. Essential and most importantly, the program must be geared to enhance functional recovery in the affected patient. The exercise training is designed as a step-by-step program to improve patients' function and optimal neutral spine posture. These programs include stabilization training to attain adequate dynamic control of lumbar spine forces and eliminate repetitive injury. Soft tissue flexibility, joint mobility, abdominal muscle strengthening, and aerobic exercise are also important factors.

Spinal manipulation is controversial and is neither recommended in patients with radiculopathy pain, nor is it wise in those for whom a diagnosis has not been established. For appropriately selected patients, if manipulation has not resulted in symptomatic and functional improvement after 4 weeks, it should be stopped and the patient reevaluated.

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B.2. What are the traditional interventional treatments available and how should they be used?

Common traditional interventional treatment includes the following:

- Trigger point injection
- Traditional epidural steroid injection (interlaminar approach)
- Transforaminal epidural steroid injection (transforaminal approach)
- Facet joint intra-articular block or medial branch block

Interventional techniques such as trigger point injections and local infiltration are used to provide pain relief of short duration, so other activities and physical therapy that might otherwise be severely limited by pain may be pursued.

Corticosteroids play an important role against inflammation and reduction of edema. Steroids injected into the epidural space have been used for treating low back pain and radiculopathy for many decades. Despite widespread use, the results of epidural steroid injection are still in question because studies evaluating the response to this therapy have been small, poorly controlled, and lacking good long-term follow-up. Published studies of the effectiveness of epidural steroid

injections have varied from 18% to 90%. The addition of hyaluronidase into the epidural injectate is thought to improve the spread of local anesthetic and steroid through tissue planes. Hyaluronidase acts by cleaving hyaluronic acid, which is found within connective tissue, skin, aorta, vitreous humor of the eye, joint cartilage, and the nucleus pulposus of the disc. Epidural steroid injections can be performed through the interlaminar route, the caudal canal, or the intervertebral foramina. The spread of solution in both caudal and interlaminar injection is less controllable because of inconsistent lateral flow into the ventral compartment. This renders the medication less effective as it is diverted away from the compartment, depending on the tightness of the lateral recess and the size of the dural sac. In normal volunteers, the transforaminal method showed good ventral flow, whereas the interlaminar approach showed predominantly dorsal flow, which was far from the usual site of impingement.

Patients who suffer from lumbar facet arthropathy may have symptoms, including band-like low back pain and associated hip, groin, or thigh pain. Pain rarely radiates below the knee in this condition. Blockade of the medial branch of the dorsal ramus of the spinal nerve or intra-articular injections of the lumbar facets are effective in short-term alleviation of this type of pain.

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B.3. What are some of the recent advances in minimally invasive interventions?

There are several recent interventional techniques for the management of low back pain and sciatica that can be applied to appropriately selected patients. These include the following:

- Epidural neuroplasty or epidural adhesiolysis
- Epiduroscopy (spinal canal endoscopy)
- Percutaneous radiofrequency denervation of medial branches for facet joint pain
- Automated percutaneous discectomy (APD) or percutaneous automated discectomy (PAD) or percutaneous automated nucleotomy (PAN)
- Percutaneous laser disc decompression (PLDD)
- Intradiscal electrothermal therapy (IDET)
- Percutaneous disc decompression using nucleoplasty
- Percutaneous lumbar discectomy using Dekompressor probe
- Spinal cord stimulation (SCS)
- Intrathecal drug delivery
- Percutaneous vertebroplasty (PV) and percutaneous kyphoplasty (PK)

Epidural neuroplasty or epidural adhesiolysis is done with hypertonic saline and hyaluronidase to lyse epidural adhesions. This technique involves placing a rigid catheter into the epidural space, with manipulation of the catheter to physically breakdown the adhesions and applying local anesthetic, steroid, hypertonic saline (10%), and hyaluronidase over several days.

Epiduroscopy (or spinal canal endoscopy) allows directly visualization of the epidural space using a flexible fiberoptic catheter. Adhesions are lysed with the catheter under direct vision; thereafter, better delivery of medications to the target area can be achieved.

Percutaneous radiofrequency denervation of the medial branches of the dorsal (or posterior) rami of segmental spinal nerves is achieved by applying heat to denature the nerves that innervate the painful facet joints. The success rate has been reported variably in the range of 17% to 90% for facet joint pain of a few weeks' to several months' duration. With this technique, the pain may return several weeks to months after the axons regenerate; repeating the procedure is then indicated.

Percutaneous manual nucleotomy was first presented by Hijikata in 1975. It was proposed as a method of preventing perineural and epidural scar formation by avoidance of entry into the spinal canal. Thereafter, APD or PAD or PAN was designed as a procedure using "nucleotome" (reciprocating suction-cutting probe) for intradiscal decompression by Onik in 1985. The cannula requires a sizable annular incision to reach the nucleus. Its success rate is approximately 70% to 80%.

PLDD is a technique, introduced by Ascher and Choy in 1987, using neodymium:yttrium-aluminum-garnet (Nd:YAGq) laser to "vaporize" a small portion of the nucleus pulposus in an attempt to decompress the involved disc. It has been demonstrated that the inner pressure of the nucleus pulposus drops significantly after the disc ablation. Its success rate is approximately 78%. After 4 to 6 months from this treatment, it was demonstrated that one-third of repeat MRI scans showed modest to moderate decrease in the size of disc herniation. There is concern, nevertheless, that the technique is potentially hazardous to bone and nerve tissue because of the significant rise in temperature resulting from thermal energy transfer.

IDET or annuloplasty, first reported by Saal and Saal in 2000, has been shown to be effective in managing discogenic pain. It is a minimally invasive procedure in which a catheter is inserted into the nucleus pulposus through which an electrode is passed so that a controlled level of heat at a temperature of 90° C (194° F) can be applied to a broad section of the affected disc inner wall. This thermal therapy is postulated to alleviate discogenic pain by shrinking collagen at a target temperature of 65° C (149° F) to 75° C (167° F). Another proposed mechanism is

denervation of exposed nociceptor endings in the outer disc annulus starting at 45° C (113° F).

Percutaneous disc decompression with nucleoplasty is used for those patients whose symptoms are attributed to radiographically contained discs, that is, disc with intact outer annulus.

Since 2000, by combining tissue removal with thermal treatment, disc decompression has been achieved. It applies a focused "coblation" technique, ablating while coagulating (by using bipolar radiofrequency) to reach the level of 40° C (104° F) to 70° C (15° F). At this temperature, molecular dissociation is achieved and thought to minimize the potential for surrounding tissue damage.

Percutaneous disc decompression using a Dekompressor probe is another option for those patients whose symptoms are attributed to radiographically contained discs. It provides objective evidence that disc was removed, the cellular character of that material, and provides a qualitative and quantitative measure.

SCS is a technique in which electrodes are passed into the posterior epidural space. Electrical stimulation of the spinal cord has been shown to be effective in the management of certain neuropathic pain syndromes and postlaminectomy syndromes. The exact mechanism by which pain relief is achieved remains controversial.

Intrathecal drug delivery directly into the cerebrospinal fluid through an implanted catheter and pump can be used to treat intractable pain from a variety of causes, both nociceptive and neuropathic. A variety of medications and combinations thereof can be used depending upon the type and location of symptoms. Among the experts, this is known as *intrathecal polyanalgesia*. This modality is indicated when increasing doses of opioid are required to achieve pain relief but at the expense of disabling side effects. The dose is effectively reduced to approximately 1/300, for example, when converting an oral dose of morphine to its equipotent equivalent delivered intrathecally.

PV and PK are both advanced techniques used in the treatment of painful compression fracture. In the United States, compression fractures occur in approximately 700,000 patients per year, and 80% of these fractures occur in women. The conventional management includes bed rest, analgesics, and bracing. PV was a technique developed in 1984 for the treatment of painful vertebral hemangiomas. It has since become popular for the treatment of osteoporotic vertebral body compression fracture. It involves the application of liquid cement (polymethylmethacrylate), tobramycin, and barium powder (as nonionic contrast) through a special metal needle inserted under fluoroscopy. The cement provides vertebral solidification and buttresses the compressed bone within the vertebral body. The procedure usually takes 45 to 60 minutes, and the patient may be discharged several hours later. Some risks are involved with this procedure, such as leakage of cement into surrounding areas (disc, spinal cord, and nerve roots), infection, bleeding, worsened pain, embolism, and paralysis. Overall, more than 80% of treated patients had moderate to marked pain relief.

PK is a recently developed technique similar to PV, which involves the additional application of an inflatable balloon inside the collapsed vertebral body. The compressed fracture is thus expanded, the lost height of the vertebral body is restored, and an inner space or cavity is created for the cement. This procedure was approved by the U.S. Food and Drug Administration in 1998. A significant reconstitution of the curvature of the spine can be seen following kyphoplasty. According to Lieberman, in 70% of the collapsed vertebral bodies, the kyphoplasty restored 47% of the lost height. This newer technique offers the additional advantage of realigning the spinal column and restoring height to the fractured vertebrae.

PV and PK are associated with pain relief in 67% to 100% of cases. Most patients experience significant pain relief within the first 1 to 2 days. There is also a report of 95% improvement in pain and significant improvement in function following treatment by either of the two techniques.

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B.4. When should surgery be considered?

Several surgeries are indicated for low back pain and sciatica. These include laminectomy, macrodiscectomy or microdiscectomy, foraminotomy, intervertebral body insertion, and spinal fusion.

According to Weber's study, the long-term results appear to be no different in the surgery versus nonsurgery group in the case of low back pain. If the following situations occur, surgery should be considered:

- Failure to respond to conservative management for at least 3 months
- A profound or progressing neurologic defect such as a complete foot drop
- Recurring episodes of intractable sciatica involving the same segment—mainly to avoid the cumulative disability of repeated events.

Muscle weakness is a dubious indication for surgery if the paresis is of unknown duration. If the pressure on the nerve root can be relieved immediately after the appearance of the paresis, surgery has been regarded as the therapy of choice. Unfortunately, most patients are unaware of the subtle loss of motor function. The greatest concern and complaints are largely centered on pain, paresthesia, and immobility.

Within the first 3 months of acute low back symptoms, surgery is considered only when serious spinal pathology or nerve root dysfunction, obviously resulting from a herniated lumbar disc, is detected. Nerve root decompression can be considered for a patient if all of the following criteria exist:

- Sciatica is both severe and disabling.
- Symptoms of sciatica persist without improvement for longer than 4 weeks or with extreme progression.
- There is strong physiologic evidence of dysfunction of a specific nerve root with intervertebral disc herniation confirmed ipsilaterally at the corresponding level by imaging.

Patients with acute low back pain alone, without findings of serious conditions or significant nerve root compression, rarely benefit from a surgical consultation. With or without surgery, more than 80% of patients with obvious surgical indications eventually recover.

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B.5. What new surgical options are now available for treatment of disc disease?

- Artificial disc replacement (ADR)
- Interspinous process decompression system (X STOP)

In the mid-1980s, Drs. Schellnack and Buttner, German orthopedic surgeons, developed a metal and plastic prosthesis that has been in clinical use for more than 17 years. The prosthesis is known as the *SB CHARITÉ*. The prosthesis design is currently in its third generation. Other prosthetic discs are available, including Prodisc, Maverick, FlexiCore, and Kineflex. In October 2004, the CHARITÉ artificial disc became the first to be approved for disc replacement in the United States. It is composed of two metallic endplates and a polyethylene core that moves between them (Figs. 49.1 to 49.4). Traditional spinal fusion does change the mechanics of the segment that is fused.

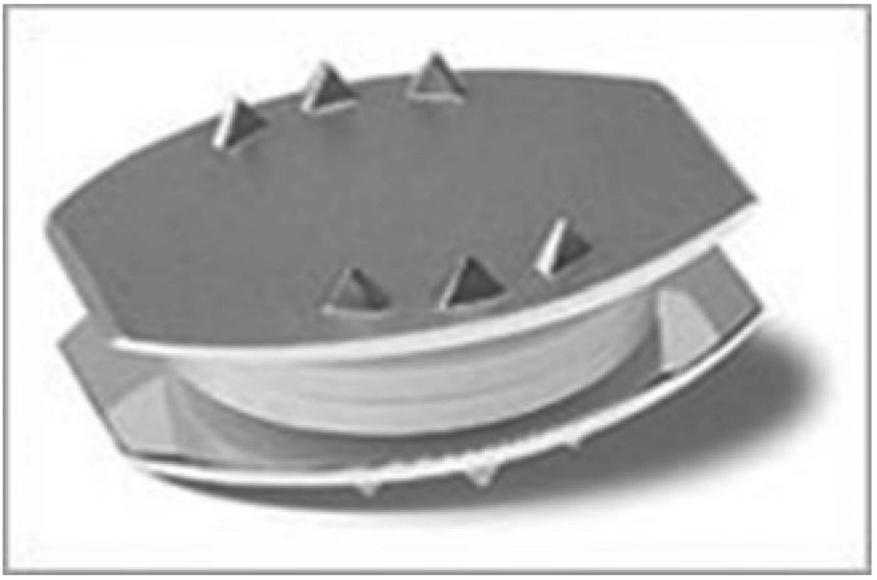

Figure 49.1 Charité disc.

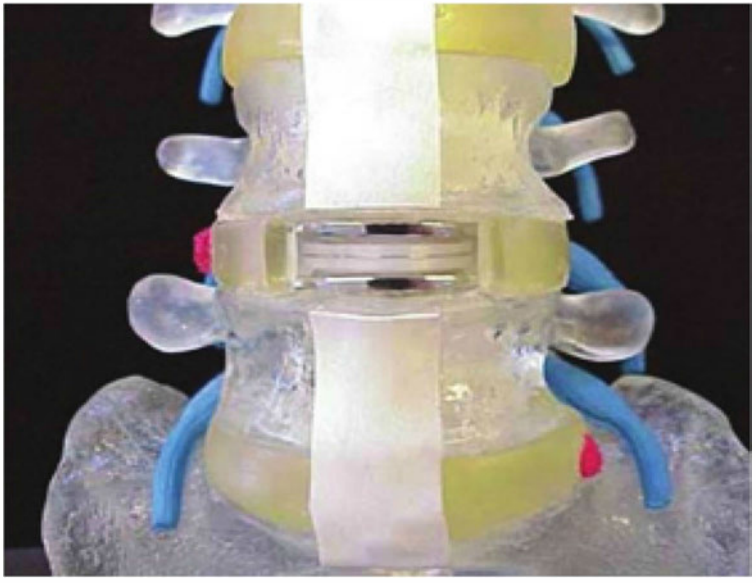

Figure 49.2 Charité disc replacement at L4-5.

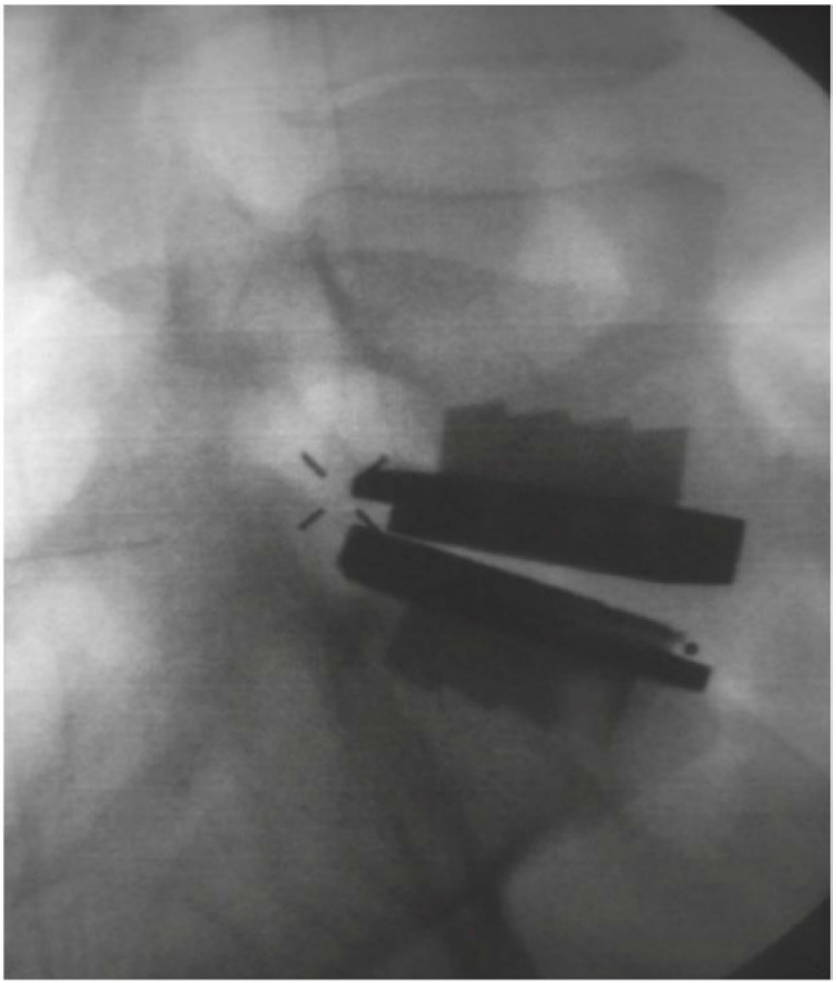

Figure 49.3 L5-S1 artificial disc replacement, lateral fluoroscopic view.

Adjacent segment degeneration can develop at approximately 3% per year (or 16.5% at 5 years, 36.1% at 10 years). One major theoretic advantage of ADR over spine fusion is that it results in no change in the biomechanics of the lower spine, thereby allowing the spine to maintain its normal range of motion and reducing or eliminating the risk for degeneration in the adjacent segments of the spine. The indications for ADR are similar to those for an anterior lumbar interbody fusion using interbody cages. The contraindications for ADR include infection, spinal stenosis, spondylolisthesis (or other types of instability in the spine, such as fracture or tumor), scoliosis, facet joint osteoarthritis, significant radiculopathy, osteoporosis, and pregnancy. Artificial discs are not perfect. The potential disadvantage of ADR is a limited durability. Because disc injury is a common cause of back pain in younger adults, an artificial disc in such patients needs to last for decades. The demands on that disc will be very great, and it may not outlast the lifetime of the patient, who may need revision surgery

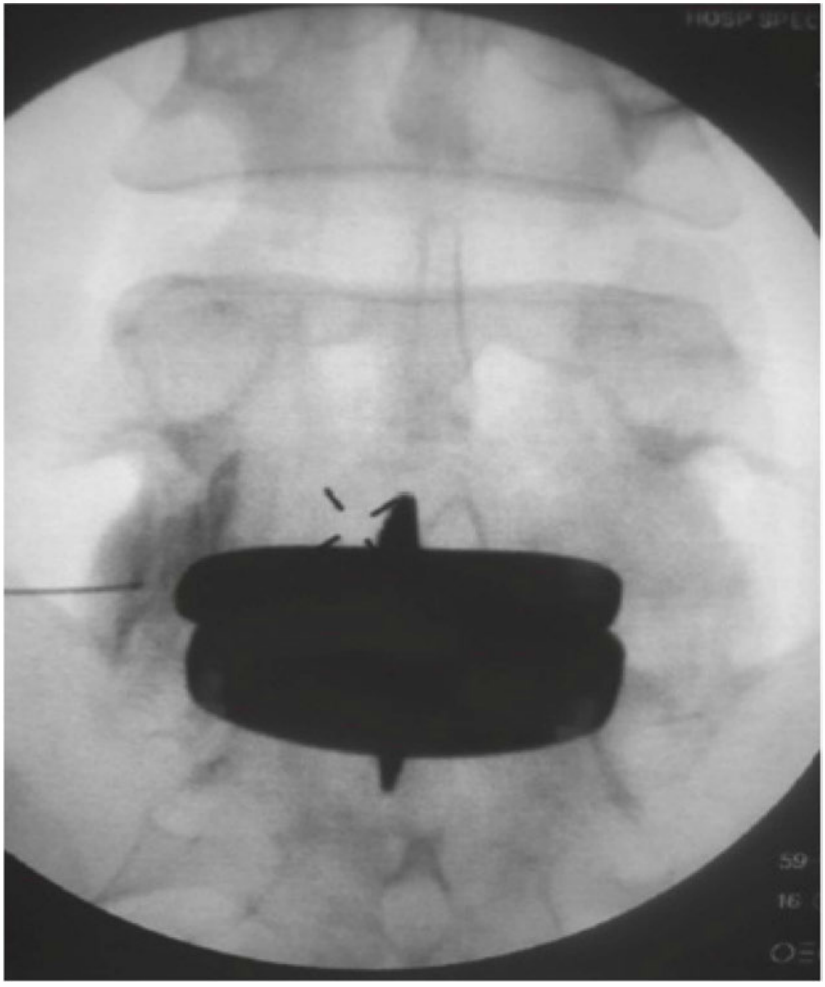

Figure 49.4 Anteroposterior fluoroscopic view of artificial disc replacement.

later. Revision ADR can be very dangerous because of scar tissue from the original surgery in nearby vascular structures. In addition, there is a 1% to 3% of complication of retrograde ejaculation in men. The recent study regarding Canadian cohort of patients demonstrated satisfactory clinical and radiographic results in a carefully selected patient population. The radiographic assessment confirmed preservation and maintenance of motion of the replaced disc (L4-5 or L5-S1) with a follow-up (2 to 7 years) averaging 55 months.

The interspinous process decompression system (X STOP) is a titanium metal implant made to fit between the lumbar spinous processes of the vertebrae (Figs. 49.5 and 49.6). It is designed to relieve narrowing of the spinal canal and neural foramen during extension, thereby reducing the symptoms of neurogenic intermittent claudication. The indications include spinal stenosis and degenerative lumbar spondylolisthesis.



Figure 49.5 Interspinous process decompression system (X STOP).

Anderson PA, Tribus CB, Kitchel SH. Treatment of neurogenic claudication by interspinous decompression: application of the X STOP device in patients with lumbar degenerative spondylolisthesis. *J Neurosurg Spine*. 2006;4:463–471.

Blumenthal SL, McAfee PC, Guyer RD, et al. A prospective, randomized investigational device exemptions study of lumbar total disc replacement with the Charité™ artificial disc versus lumbar fusion: part I: evaluation of clinical outcomes. *Spine*. 30:1565–1575.



Figure 49.6 Interspinous process decompression system (X STOP).

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Katsimihas M, Bailey CS, Issa K, et al: Prospective clinical and radiographic results of CHARITE III artificial total disc arthroplasty at 2- to 7-year follow-up: a Canadian experience. *J Can Chir*. 2010;53:408–414.

Kulkarni V, Rajshekhar V, Raghuram L. Accelerated spondylotic changes adjacent to the fused segment following central cervical corpectomy: magnetic resonance imaging study evidence. *J Neurosurg*. 2004;100:2–6.

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Zucherman JF, Hsu KY, Hartjen CA, et al. A multicenter, prospective, randomized trial evaluating the X STOP interspinous process decompression system for the treatment of neurogenic intermittent claudication: two-year follow-up results. *Spine*. 2005;1530:1351–1358.

CHAPTER 50

Perioperative Pain Management

Anuj Malhotra, Vinod Malhotra, and Narinder Rawal

A 60-YEAR-OLD-MAN

with a smoking history of a pack of cigarettes a day for approximately 40 years and chronic obstructive pulmonary disease is scheduled for thoracotomy for removal of carcinoma in his right middle lobe.

A. Perioperative Pain Management for Thoracotomy

1. What would be your advice to the patient about the planned thoracotomy and postoperative pain relief?
2. How will you decide about the choice of anesthetic technique?
3. What is chronic postthoracotomy pain syndrome (PTPS)? Does video-assisted thoracic surgery reduce the risk of chronic pain after thoracotomy?
4. What would be your perioperative analgesic strategy?
5. Does the choice of analgesic technique influence postoperative outcome?
6. Does it matter if the epidural catheter is at the thoracic or lumbar level?
7. Does the choice of drugs influence the efficacy or safety of thoracic epidural analgesia (TEA)?
8. What are the usual doses and concentrations of the anesthetic combinations commonly employed in epidural analgesia?
9. If accidental dural puncture occurs during placement of the epidural needle, what steps should be taken?
10. What are the alternatives to TEA?
11. What is the usual clinical regimen for intravenous patient-controlled analgesia (IV-PCA) and is special patient monitoring required during its use?
12. What are the side effects and complications of epidural technique?
13. What recommendations for placement and removal of the epidural catheter will you make if this patient is on antiplatelet or anticoagulant therapy or thromboprophylaxis is planned?

A 70-YEAR-OLD WOMAN

with metastatic breast cancer has been treated for the last 6 months with transdermal fentanyl (Duragesic patch) for her cancer pain. She is currently on a 100-μg per hour patch every 72 hours. She is now scheduled for surgery for hip fracture after a fall. The patient was very dissatisfied with postoperative pain management after her breast surgery 3 months earlier.

B. Chronic Opioid Therapy and Perioperative Pain Management

1. How does chronic opioid therapy influence postoperative pain management?
2. What are the causes for increased postoperative pain and opioid consumption in patients chronically using opioids?
3. What are the main differences between a chronic opioid-consuming patient and a patient who abuses or is addicted to opioids?
4. What issues need to be considered in the opioid-tolerant patient who is scheduled for surgery?
5. What would be your strategy regarding preoperative information and choice of anesthesia technique?
6. What are the choices for perioperative pain management in opioid-tolerant patients?
7. What issues need to be considered before discharging an opioid-tolerant patient?

A 38-YEAR-OLD WOMAN

scheduled for ambulatory laparoscopic cholecystectomy requests to see the anesthesiologist preoperatively to discuss her postoperative analgesia strategy. She experienced severe pain at home for several days after a previous ambulatory laparoscopic gynecologic procedure.

C. Perioperative Pain Management for Ambulatory Surgery

1. What would be your preoperative considerations and advice to the patient?
2. What are the consequences of inadequate pain management after ambulatory surgery?
3. What is the role of premedication or preoperative analgesic?
4. Does the choice of anesthetic technique influence postoperative pain?
5. Are nonsteroidal anti-inflammatory drugs (NSAIDs) effective? If so, does the choice of drug matter?
6. There are three types of pain after laparoscopic cholecystectomy: incisional, subphrenic, and shoulder pain. What is the role of surgical technique in influencing postoperative pain?
7. What would be your strategy for pain control after discharge home?

MANY PATIENTS

continue to experience moderate to severe pain after surgery. What can we do to address this long-standing problem?

D. The Role of an Acute Pain Service

1. What is the extent of the problem and which patients are at the greatest risk of undertreatment?
2. What are the consequences of inadequate postoperative pain relief?
3. What is the role of an acute pain service (APS) in improving postoperative pain management?
4. Does an APS improve postoperative outcome?

A. Perioperative Pain Management for Thoracotomy

A.1. What would be your advice to the patient about the planned thoracotomy and postoperative pain relief?

It is essential that patients undergoing thoracotomy be informed about what to expect after surgery because an understanding of the procedure as well as realistic expectations of pain and rehabilitation can promote recovery and return to normal activity. Patients undergoing thoracotomy may suffer from severe acute postoperative pain if analgesia is not managed appropriately. Pulmonary function is impaired as a result of thoracic surgery, and may be worsened by the effects of pain. Therefore, during the early postoperative period, pain control and maintenance of pulmonary function are the major goals. For preoperative improvement of pulmonary function, patients should be advised to stop smoking and be instructed in deep breathing exercises such as incentive spirometry.

Online educational resources, such as http://www.asahq.org/For-the-Public-and-Media.aspx and http://www.lifelinetomodernmedicine.com/faqs.aspxcan, also help inform patients about their forthcoming anesthetic procedure and provide specific advice about the different anesthetic and pain relief techniques for surgery.

Early postoperative pain may be intense and can delay rehabilitation and mobilization unless appropriately treated. Different techniques may be used to manage different levels of pain immediately following surgery, within the first few postoperative days, and thereafter. Pain management often involves a step-down approach from regional anesthesia or systemic opioids to oral medication. The following issues need to be addressed:

- Information must be given on the hospital policy for pain assessment, for example, the use of visual analog scores.
- Patients require a realistic expectation of the intensity and duration of postoperative pain.
- Pain management techniques that require patient involvement (intravenous patient-controlled analgesia (IV-PCA), patient-controlled epidural analgesia) need to be properly demonstrated.
- Online information resources, such as the PROSPECT (PROcedure SPECific postoperative pain managemenT) guidelines and recommendations by an international panel of anesthesiologists and surgeons available at http://www.postoppain.org, may be of use.

A.2. How will you decide about the choice of anesthetic technique?

The decision about which anesthetic technique to use for an individual patient is based on a review of their overall medical condition and any medications that they are taking. General anesthesia with or without epidural may be selected based on the patient's comorbidities and the planned procedure. Because lung volumes after thoracic surgery may be reduced by up to 50% through a combination of resection and splinting atelectasis, an epidural can have benefit not only for pain relief but also for improving pulmonary function. Other factors such as surgical and anesthetic experience and practice, local ward or institutional protocols for postoperative pain relief, and patient mobilization will also influence the choice of anesthetic technique. If an epidural is included in the anesthetic plan, it may be inactive throughout the case, used as an adjunct to general anesthesia, or bolused at the end of the case prior to a postoperative infusion. Again, this decision is often based on patient and surgical considerations, such as potential blood loss, hypotension, and invasiveness of surgery. Intraoperative epidural use prior to wake up has the benefit of ensuring epidural catheter function and can facilitate a more comfortable transition to the immediate postoperative period.

The use of intraoperative and postoperative thoracic epidural technique has become widely used for management of pain associated with thoracic and major abdominal surgery. Clinical studies have shown that thoracic epidural anesthesia can have effects far beyond pain relief, including decreased opioid consumption, reduced risk of nausea and vomiting, increased lung volumes, reduced risk of pulmonary complications, improved bowel recovery, and a significant reduction in the incidence of myocardial infarction. There is also evidence that neuraxial block decreases the risk of recurrence after cancer resection, likely through an opioid-sparing effect.

Ballantyne JC, Carr DB, DeFerranti S, et al. The comparative effects of postoperative analgesia therapies on pulmonary outcome: cumulative meta-analyses of randomized, controlled trials. *Anesth Analg*. 1998;86(3):598–612.

Beattie WS, Badner NH, Choi P. Epidural analgesia reduces postoperative myocardial infarction: a meta-analysis. *Anesth Analg*. 2001;93(4):853–858.

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Christopherson R, James KE, Tableman M, et al. Long-term survival after colon cancer surgery: a variation associated with choice of anesthesia. *Anesth Analg*. 2008; 107:325–332.

Exadaktylos AK, Buggy DJ, Moriarty DC, et al. Can anesthetic technique for primary breast cancer surgery affect recurrence or metastasis? *Anesthesiology*. 2006;105:660–664.

Jørgensen H, Wetterslev J, Møiniche S, et al. Epidural local anaesthetics versus opioid-based analgesic regimens for postoperative gastrointestinal paralysis, PONV and pain after abdominal surgery 2001. *Cochrane Database Syst Rev*. 2001;CD001893. doi:10.1002/14651858.CD001893.

A.3. What is chronic postthoracotomy pain syndrome (PTPS)? Does video-assisted thoracic surgery reduce the risk of chronic pain after thoracotomy?

Chronic PTPS is defined as pain that recurs or persists along a thoracotomy scar at least 2 months after surgery and is not related to the recurrence of a tumor or an infection. PTPS is generally neuropathic in nature and varies in severity, with a reported incidence of 44% to 80%. Several studies suggest that poor perioperative pain management contributes to chronic PTPS and that aggressive management of early postoperative pain with epidural analgesia can reduce its incidence.

Although used with increasing frequency, thoracoscopic approaches have not had the favorable impact on pain that many had anticipated. Surprisingly, video-assisted thoracic surgery is associated with a prevalence of chronic pain comparable to that of open procedures, with rates of PTPS ranging from 22% to 63%, likely due to intercostal nerve and muscle damage from trocar insertion.

Bertrand PC, Regnard JF, Spaggiari L, et al. Immediate and long-term results after surgical treatment of primary spontaneous pneumothorax by VATS. *Ann Thorac Surg*. 1996;61:1641–1645.

Gottchalk A, Cohen SP, Yang S, et al. Preventing and treating pain after thoracic surgery. *Anesthesiology*. 2006;104:594–600.

International Association for the Study of Pain, Subcommittee of Taxonomy. Classification of chronic pain. *Pain*. 1986;24(suppl 3):S138–S139.

Katz J, Jackson M, Kavanagh BP, et al. Acute pain after thoracic surgery predicts long-term post-thoracotomy pain. *Clin J Pain*. 1996;12(1):50–55.

Landreneau RJ, Mack MJ, Hazelrigg SR, et al. Prevalence of chronic pain after pulmonary resection by thoracotomy or video-assisted thoracic surgery. *J Thorac Cardiovasc Surg*. 1994;107:1079–1085.

Ng JM, Hartigan PM. Pain management strategies for patients undergoing extrapleural pneumoectomy. *Thorac Surg Clin*. 2004;14:585–592.

Perttunen K, Tasmuth K, Kalso E. Chronic pain after thoracic surgery: a follow-up study. *Acta Anaesthesiol Scand*. 1999;43(5):563–567.

Senturk M, Ozcan PE, Talu GK, et al. The effects of three different analgesia techniques on long-term postthoracotomy pain. *Anesth Analg*. 2002;94(1):11–15.

Tiippana E, Nilsson E, Kalso E. Post-thoracotomy pain after thoracic epidural analgesia: a prospective follow-up study. *Acta Anaesthesiol Scand*. 2003;47(4):433–438.

A.4. What would be your perioperative analgesic strategy?

The analgesic plan should consider the entire perioperative period. A multimodal approach would be preferable to account for the multiple pathways by which nociceptive input is conveyed to the central nervous system, the number of pharmacologically distinct mechanisms of modulating this input, the need for effective analgesia throughout the perioperative period and after discharge, and the importance of minimizing side effects, particularly respiratory depression.

Thoracic epidural analgesia (TEA) is the mainstay of recommended therapy for the reasons previously discussed. Contraindications to a thoracic epidural include patient refusal, coagulopathy, thrombocytopenia, therapeutic anticoagulation, previous thoracic spine surgery, and local infection over the entry site. When epidural catheters fail intraoperatively or have patchy coverage, intercostal nerve blocks (ICNBs) or paravertebral blocks may supplement epidural analgesia or serve as a bridge to the immediate postoperative period when an epidural catheter can be safely replaced.

Intravenous nonsteroidal anti-inflammatory drugs (NSAIDs) are useful for treating shoulder pain secondary to referred diaphragmatic pain. This nociceptive input is carried by vagal and phrenic nerves and is often refractory to epidural analgesia. A concern with NSAIDs is platelet dysfunction; however, so long as the bleeding risk is reasonable, their efficacy and lack of respiratory side effects makes them an optimal choice for adjunct analgesia. Cyclooxygenase 2 (COX-2) inhibitors have limited effects on platelets aggregation and comparable efficacy to traditional NSAIDs and thus may be of use in this setting. Adverse cardiac side effects are unlikely with short-term perioperative dosing. Regular administration of paracetamol or acetaminophen may also be useful for treating shoulder pain and can be used in addition to NSAIDs.

When making the transition to oral opioid analgesics from epidural analgesia, the first oral dose should be administered prior to discontinuing the epidural and the epidural dose should be weaned down slowly to ensure adequate coverage with an oral regimen.

Gottchalk A, Cohen SP, Yang S, et al. Preventing and treating pain after thoracic surgery. *Anesthesiology*. 2006;104:594–600.

PROSPECT *(www.postoppain.org)*

A.5. Does the choice of analgesic technique influence postoperative outcome?

Evidence strongly suggests that epidural analgesia is associated with lower rates of perioperative morbidity and, in particular, fewer pulmonary and cardiac complications. Compared with systemic opioids, epidural opioids decreased the incidence of postoperative atelectasis,increased $Pa0_2$, and decreased the incidence of pulmonary infections and pulmonary complications overall. Effective pain control with an epidural technique leads to improved pulmonary function, more effective coughing, earlier mobilization, and improved cooperation with respiratory physiotherapy.

Postoperative myocardial infarction rates are reduced when TEA is incorporated into anesthesia and extended at least 24 hours into the postoperative period. Supraventricular tachyarrhythmias, which are the most common form of cardiac morbidity after pulmonary resection and occur in up to 50% of cases, are reduced by TEA, even when compared with alternative analgesic regimens that confer equivalent pain control. The cardioprotective mechanism of TEA is believed to relate to its sympatholytic effects.

A recent meta-analysis also found that epidural analgesia provided superior postoperative analgesia compared with IV-PCA. As discussed earlier, better postoperative pain relief decreases the likelihood of developing chronic postsurgical pain.

Dworkin RH, McDermott MP, Srinivasa R. Preventing chronic postsurgical pain: how much of a difference makes a difference? *Anesthesiology*. 2010;112(3):516–518.

Wu CL, Cohen SR, Richman JM, et al. Efficacy of postoperative patient-controlled and continuous infusion epidural analgesia versus intravenous patient-controlled analgesia with opioids: a meta-analysis. *Anesthesiology*. 2005;103(5):1079–1088; quiz 1109–1110.

A.6. Does it matter if the epidural catheter is at the thoracic or lumbar level?

TEA is currently the standard for analgesia for thoracic surgery and, in the absence of contraindications, all patients undergoing major open thoracic surgical procedures should have a thoracic epidural catheter placed preoperatively. The tip of the catheter should reside at the dermatome along which the incision will be made.

Thoracic (versus lumbar) placement of the epidural catheter is dose saving and decreases side effects such as hypotension and bladder dysfunction at equianalgesia. Thoracic placement also reduces motor block of the lower extremities, which allows for improved postoperative ambulation. However, if thoracic epidural placement is contraindicated or cannot be achieved, lumbar epidural anesthesia can be utilized. Lumbar placement can be efficacious, particularly when used with hydrophilic opioids such as morphine; however, local anesthetic volume dosing is significantly higher and may be limited by toxicity.

Grant GJ, Zakowski M, Ramanthan S, et al. Thoracic versus lumbar administration of epidural morphine for postoperative analgesia after thoracotomy. *Reg Anesth*. 1993;18:351–355.

Sandler AN, Stringer D, Panos L, et al. A randomized, double-blind comparison of lumbar epidural and intravenous fentanyl infusions for postthoracotomy pain relief: analgesic, pharmacokinetic, and respiratory effects. *Anesthesiology*. 1992;77:626–634.

A.7. Does the choice of drugs influence the efficacy or safety of thoracic epidural analgesia (TEA)?

Effective postoperative pain control may be achieved by delivering an opioid, local anesthetic, or a combination of both into the thoracic epidural space. Combinations are the standard because synergy between opioids and local anesthetic agents can enable an optimum balance between analgesia and minimizing blockade of motor function of the thorax and dynamic consequences of sympatholysis. Common components include opioids such as morphine, fentanyl, or sufentanil, and local anesthetic agents such as bupivacaine, levobupivacaine, or ropivacaine. Systemic absorption effects (e.g., sedation) tend to be more common with the lipophilic opioids, such as fentanyl, presumably because of increased absorption into the epidural fat. Hydrophilic opioids, such as morphine, produce a wider dermatomal band of analgesia with less systemic absorption. Of the three commonly used local anesthetic agents, bupivacaine possesses the least favorable cardiac safety profile. In theory, ropivacaine offers the advantage of differential dose-dependent sensory and motor blockade; however, when used in dilute concentrations in combination with opioids, it is unlikely that any advantage of one agent over the other will be apparent.

Ng JM, Hartingan PM. Pain management strategies for patients undergoing extrapleural pneumonectomy. *Thorac Surg Clin*. 2004;14:585–592.

Rawal N. Intraspinal opioids. In: Rowbotham DJ, Macintyre PE, eds. *Acute Pain*. London: Arnold; 2003:241–266.

A.8. What are the usual doses and concentrations of the anesthetic combinations commonly employed in epidural analgesia?

Before the initiation of patient-controlled epidural analgesia, a test dose of 3 mL of 1.5% lidocaine with epinephrine 1:200,000 is usually employed to rule out intrathecal or intravascular placement of catheter. Once malposition is ruled out, the catheter is usually bolused (as allowed by hemodynamic status) prior to beginning continuous infusion.

Commonly employed combinations of epidural drugs vary from institution to institution. However, in the interest of patient safety, compliance, auditing, and quality assurance, standardization within the institution is recommended. Solutions and volumes can later be titrated to effect or to avoid side effects, for example, increasing or decreasing local anesthetic concentration to change block density, increasing or decreasing volume infused to increase spread, and adding or subtracting opioids to increase analgesia or decrease side effects such as itching, nausea, or vomiting.

At our institution, the following drugs and drug combinations are used at an infusion rate of 4 mL per hour with each demand bolus of 3 mL as needed.

- Bupivacaine 0.0625% with fentanyl 5 μg per mL with a lockout period of 10 minutes between boluses
- Fentanyl 10 μg per mL with a lockout period of 10 minutes

- Bupivacaine 0.0625% with dilaudid 100 μg per mL with a lockout period of 20 minutes
- Morphine sulphate 100 μg per mL with a lockout period of 30 minutes

(See Sample Order Form [Fig. 50.1].)

A.9. If accidental dural puncture occurs during placement of the epidural needle, what steps should be taken?

If accidental dural puncture occurs during placement of epidural needle, the general practice is to remove the needle and place the epidural catheter at adjacent intervertebral spaces. The likelihood of intrathecal spread should be carefully assessed with the test dose. Epidural infusion may be started at the usual rate. Frequent monitoring for sensory and sympathetic block should continue in a controlled setting until the efficacy and safety of the epidural analgesia is established. In addition, the patient should be assessed for any symptoms of neuropathy relevant to the level attempted. The patient should be informed of the dural puncture and the potential for postdural puncture headache.

A.10. What are the alternatives to TEA?

There are times when for technical, medical, or other reasons thoracic epidural catheter placement is unsuccessful, undesirable, or not possible. Alternatives to mid-TEA include lower thoracic and lumbar epidural catheter placement, ICNBs, paravertebral blocks, intrathecal opioids, intrapleural catheters, local anesthetic infiltration, and systemic analgesia with one or more agents.

Lumbar epidural placement can be efficacious, particularly when used with hydrophilic opioids such as morphine to increase dermatomal spread. Lumbar epidurals are most limited by the need for increased local anesthetic dosing and the higher incidence of side effects such as hypotension and urinary retention versus thoracic epidurals.

If epidural placement is ruled out altogether for the reasons previously discussed, ICNBs can be performed percutaneously or under direct vision intraoperatively, using single injections or placement of an intercostal catheter. While often initially effective, unpredictable spread of local anesthetic and rapid local anesthetic absorption by surrounding vessels make this technique less effective than epidural analgesia. Furthermore, indwelling intercostal catheters cannot adequately control pain after posterolateral thoracotomy because posterior primary rami and sympathetic fibers are not blocked. Additionally, percutaneous positioning and securing of intercostal catheters may be technically problematic.

Paravertebral block results in ipsilateral somatic and sympathetic nerve blockade in multiple contiguous thoracic dermatomes above and below the site injection. Paravertebral analgesia has been found to produce good pain relief and preservation of pulmonary function after thoracotomy and is probably the best available alternative to epidural analgesia. Because the concomitant sympathetic blockade is unilateral, the incidence of adverse effects, such as hypotension and urinary retention, is lower. Paravertebral blocks can be performed as single injections or through a paravertebral catheter. Paravertebral catheters can be placed percutaneously or intraoperatively under direct vision and are more suitable than epidural catheters when coagulopathy is of concern. In some studies, paravertebral blocks have been shown to be as effective as TEA with respect to pain control and preservation of pulmonary function after thoracotomy.

A preoperative single bolus of spinal morphine as part of multianalgesic regimen can be considered in order to decrease the need for systemic opioids. Alternatively, pleural catheters may be placed intraoperatively to decrease pleural and visceral pain; however, they do not affect incisional pain and require high volumes of local anesthetic to be effective. Similarly, direct local anesthetic infiltration can be used

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EPIDURAL ANALGESIA ORDER SHEET
PAIN MANAGEMENT

IF NO PLATE, PRINT NAME, SEX AND MEDICAL RECORD NO.

DATE: / / TIME: am/pm	ORDER POSTED	CHECKED BY RN
1) Analgesia by epidural infusion (using the PCA infuser).		
2) The patient **MUST NOT** receive any supplemental narcotics, sedatives and/or antiemetics while receiving Epidural Analgesic unless orders are written by the Pain Management Service.		
3) Narcotic (Specify drug, # of mgs, volume, and diluent and concentration):		
4) Initial Bolus given by Pain Service M.D. (Dose given _____)ml		
5) Initial Machine Settings: **Epidural Mode** (circle one) Continuous / Bolus / Both Program in ml. a) **Program in ml.** b) Bolus/Demand Dose _____ ml per attempt. c) Bolus/Demand Lockout _____ minutes. d) Continuous Rate _____ ml per hour. e) Limit _____ ml per four hours.		
6) If pain is not controlled at the above settings (pain ≥ 6), the nurse may administer a PRN rescue / loading dose_____ml every 10 minutes until the patient is comfortable. The maximum rescue / loading dose is_____ml Increase pump settings to: a) Bolus/Demand Dose _____ ml per attempt. b) Bolus/Demand Lockout _____ minutes. c) Continuous Rate _____ ml per hour. d) Limit _____ ml per four hours.		
7) A) For oversedation (sedation scal ≥ 4/R4) and respiratory rates 10–14 minute, notify Acute Pain Service, and decrease pump settings to: a) Bolus/Demand Dose _____ ml per attempt. b) Bolus/Demand Lockout _____ minutes c) Continuous Rate _____ ml per hour. d) Limit _____ ml per four hours B) For respiratory rate less than 10/minute, stop infusion and call the Acute Pain Servive (X-66700, beeper 16664). C) For respiratory rate less than 8/minute, obtain naoxone (0.4 mg/ml and administer 0.1 mg (0.25 ml) IV bolus q2 minutes until respiratry rate is 8/minute or greater, stop Infusion, and notify Pain mangement Service (X-66700, beeper 16664).		
8) Upon initiation and after every loading dose, obtain BP, pulse, respiratory rate, sedation scale and sensory motor function q30 min × 2 hours then q1 h × 2 then q4 hours. Pain analog q4 hours, Temp q12 hours).		
9) If no maintenance IV solution is ordered, IV to med lock.		
10) For Nausea (Specify drug and dosing):		
11) For Sleep (Specify drug and dosing):		
12) Activity level per surgical/medical orders.		
13) For questions or problems, call the Pain Management Service at X-62960 or page: X-66700, beeper 16664.		
14) Please call Unit Coordinator when the pump is discontinued.		

M.D Signature Print Name Code Beeper Number

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Figure 50.1 Epidural analgesia order sheet.

but must be combined with longer-acting strategies to provide adequate pain control. Although systemic opioids have been well documented to reduce postthoracotomy pain, their adverse effects on the respiratory system after general anesthesia, even using patient-controlled delivery systems, and their inability to provide optimal dynamic pain relief favor regional anesthetic techniques, when possible, in thoracotomy patients. Systemic analgesics are best suited as adjuncts to these techniques, and should become the mainstay of analgesic therapy only when invasive approaches are discontinued.

Cohen E, Neustein SM. Intrathecal morphine during thoracotomy, part I: effect on intraoperative enfluence requirements. *J Cardiothorac Vasc Anesth.* 1993;7(2):1546.

Debreceni G, Molnar Z, Szelig L, et al. Continuous epidural or intercostal analgesia following thoracotomy: a prospective randomized double-blind clinical trial. *Acta Anaesthesiol Scand.* 2003;47:1091–1095.

Etches RC. Respiratory depression associated with patient-controlled analgesia: a review of eight cases. *Can J Anaesth.* 1994;41(2):125–132.

Liu N, Kuhlman G, Dalibon N, et al. A randomized, double-blinded comparison of intrathecal morphine, sufentanil and their combination versus IV morphine patient-controlled analgesia for thoracotomy pain. *Anesth Analg.* 2001;92(1):31–36.

Neustein SM, Cohen E. Intrathecal morphine during thoracotomy, part II: effect on postoperative meperidine requirements and pulmonary function tests. *J Cardiothorac Vasc Anesth.* 1993;7(2):1579.

Perttunen K, Nilsson E, Heinonen J, et al. Extra-dural, paravertebral and intercostal nerve blocks for post-thoracotomy pain. *Br J Anaesth.* 1995;75:541–547.

A.11. What is the usual clinical regimen for intravenous patient-controlled analgesia (IV-PCA) and is special patient monitoring required during its use?

Clinical regimens for IV-PCA vary among institutions but the two most commonly used opioids are morphine and dilaudid. Continuous delivery, or basal rate, of the drug is commonly avoided to decrease the likelihood of respiratory depression. Boluses of morphine sulfate 2 mg or dilaudid 0.2 mg are given per demand with a lockout period of 10 minutes. Incremental boluses may be given by the nurse if pain is not controlled. The dose may be decreased or the opioid may be discontinued if respiratory depression occurs. Close monitoring and rescue strategies must be in place to ensure patient safety, particularly for at-risk individuals, including central monitoring of oxygenation and ventilation. (See Sample Order Form [Fig. 50.2].)

A recent workshop of the Anesthesia Patient Safety Foundation (APSF) looked at the issue of dangers of postoperative opioids. The workshop was held in October 2006 and focused on the issue of improved detection of postoperative opioid-induced respiratory depression. The premise of the workshop was that "the available evidence suggests that there is a significant and underappreciated risk of serious injury from PCA and neuraxial opioids in the postoperative period." The observed incidence of respiratory depression in these cases is 0.1% to 1.0% and increases to 3.2% in those older than 80 years. Patients with obstructive sleep apnea and the elderly are understandably at a higher risk of opioid-induced respiratory depression, but there is also a low and unpredictable incidence of life-threatening respiratory depression in young, healthy patients. The workshop highlighted the argument that in the United States, The Joint Commission's emphasis on pain as the "fifth vital sign" has had the unintended consequence of creating an expectation among patients that they will have little to no pain after surgery. As a result, more patients may be receiving inappropriate amounts of analgesics to meet this expectation. The conclusions of the

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PATIENT CONTROLLED ANALGESIA (PCA) ADULT ORDER SHEET

IF NO PLATE, NAME, SEX AND MEDICAL RECORD NO.

DATE: / / TIME: am/pm	ORDERED POSTED	CHECKED BY RN
1) Analgesia by Patient Controlled Analgesia (PCA).		
2) The patient **MUST NOT** receive any supplemental narcotics, sedatives and/or antiemetics while receiving PCA unless approved the Pain Management Service or House Officer		
3) Narcotics (Specify drug, # of mgs, volume, and diluent)		
4) Initial Loading: Dose_____mg every 5 minutes until the patient is comfortable. Maximum total load_____mg.		
5) Initial Machine Settings: **PCA Mode** (circle one) Continous / PCA / Both a) **Program in mg.** b) Continous Rate_____mg per hour. c) PCA Dose_____mg per demand. d) PCA Lockout_____minutes. e) Limit_____mg per four hours.		
6) If pain is not controlled at the above settings (pain ≥ 6), the nurse may administer a PRN recue / loading dose_____every 5 minutes until the patient is comfortable. The maximum rescue / loading dose is_____mg. Increase pump settings to: a) PCA Dose_____mg per demand. b) Continous Rate_____mg per hour. c) PCA Lockout_____minutes. d) Limit_____mg per four hours.		
7) For over sedation (sedation ≥ 4/R4) and respiratory rate < 14, decrease pump settings to: a) PCA Dose_____mg per demand. b) Continous Rate_____mg per hour. c) PCA Lockout_____minutes. d) Limit_____mg per four hours. For respiratory rate of 10 or lowrer, stop the pump and call the Pain Management Service (X66700, beeper 16664) or House Officer.		
8) Upon initiation, and after every loading dose given, obtain respiratory rate, heart rate and blood pressure. Repeat qh X 2, q4h X 3, and then heart rate and blood pressure per unit routine or as otherwise ordered. Monitor repiratory rate, pain analog and sedation scale q4h.		
9) Note: For patients who receive intrathecal/Epidural Morphine intraoperatively and have PCA initiated within 12 hours, monitor blood pressure, pulse, respiratory rate, pain analog/sedation q30minutes X 2h, qh X2 and then q4 hours X3, Then, BP per unit routine, Monitor respiratory rate, pain analog/sedation of 4hr.		
10) If no maintenance IV is odered, infuse D5 1/2NS at 40 ml/h via PCA Extension Set.		
11) For Nausea (Specify drug and dosing):		
12) For Sleep (Specify drug and dosing):		
13) For questions or problems, call the Pain Management Service at X62960 or page X66700, beeper 16664		
14) Please call the Unit Coordinator when the pump is discontinued. 15)		

M.D. Signature Print Name Code Beeper Number

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Figure 50.2 Patient-controlled analgesia (PCA) adult order sheet.

Anesthesia Patient Safety Foundation committee were that continuous monitoring of oxygenation and ventilation can prevent patient harm; any monitoring system should be centrally linked so that a healthcare professional can be summoned in a timely manner; programs should be instituted to educate providers and patients about the risks of opioid-associated life-threatening respiratory depression; governmental agencies and nongovernmental entities should provide increased support for scientific research in this area; and while treatment of postoperative, opioid-induced depression is an important consideration, prevention may be the more effective strategy.

Weinger MB. Dangers of post operative opioids. APSF workshop and white paper address prevention of postoperative respiratory complications. *APSF Newsl Winter*. 2006–2007;21(4):61–67.

A.12. What are the side effects and complications of epidural technique?

Depending on the extent of blockade, TEA interferes with sympathetic outflow and produces hypotension through cardiodepressant action (blockade of cardiac accelerator fibers) and a reduction in systemic vascular resistance (blockade of sympathetic chain). The use of dilute local anesthetic solutions has led to clinically insignificant motor blockade while maintaining adequate sensory block, though some small-muscle weakness may be observed. Opioid-related side effects include sedation, nausea and vomiting, pruritus, delayed gastrointestinal motility, urinary retention, and respiratory depression. The incidence of delayed respiratory depression after administration of epidural opioids is very low, and epidural opioid analgesia can be used safely on hospital wards. All patients who receive epidural analgesia should have standard orders for the treatment of breakthrough pain and side effects.

The overall catheter-related complication rate is low and includes such complications as dural puncture, unsuccessful catheter placement, paresthesia, and neurologic injury. Paraplegia associated with epidural analgesia may result from epidural hematoma, or less commonly epidural abscess. The potentially catastrophic complications of epidural or intrathecal hematoma are best prevented by realization that motor blockade should not occur with dilute local anesthetic solutions, and postoperative motor weakness should trigger immediate imaging evaluation (MRI) and neurosurgical consultation. Clearly, significant concerns about coagulopathy or local overlying infection should limit epidural catheter placement.

Rawal N. Intraspinal opioids. In: Rowbotham DJ, Macintyre PE, eds. *Acute Pain*. London: Arnold; 2003:241–266.

A.13. What recommendations for placement and removal of epidural catheter will you make if this patient is on antiplatelet or anticoagulant therapy or thromboprophylaxis is planned?

On the basis of current practice and the third consensus statement for Regional Anesthesia in the Patient Receiving Antithrombotic or Thrombolytic Therapy developed by the American Society of Regional Anesthesia, the following guidelines may be helpful.

Prophylactic unfractionated heparin

In the setting of twice-daily subcutaneous prophylaxis with 5,000 U heparin, there is no contraindication to the use of neuraxial techniques. For patients receiving greater than 10,000 U daily or thrice-daily dosing, data are insufficient to determine if there is increased risk of hematoma. These patients should have individual risk/benefit

assessments, and techniques to facilitate detection of hematoma (increased monitoring, dilute local anesthetic solutions) should be implemented. The clinician should keep in mind that subcutaneous heparin reaches peak effect 1 to 2 hours after administration.

Recommendations

- First dose of subcutaneous heparin should ideally be administered *after* block placement. Heparin dosing should be delayed at least 1 hour after epidural catheter placement.
- If the patient is already receiving prophylactic heparin, there is no contraindication to block placement. Some clinicians advocate delaying puncture 2 hours after the last dose.
- Because heparin-induced thrombocytopenia may occur during heparin administration, patients receiving heparin for more than 4 days should have a platelet count checked before neuraxial block placement and prior to catheter removal.
- An epidural catheter may be removed at any time. Some clinicians advocate waiting 2 hours after the last dose.

Therapeutic intravenous unfractionated heparin

Neuraxial techniques combined with intraoperative anticoagulation (excluding the full anticoagulation of cardiac surgery) are acceptable with certain precautions as described in the subsequent text.

Recommendations

- Neuraxial techniques should be avoided in patients with baseline coagulopathies in addition to heparinization.
- Risk/benefit determinations are needed in patients receiving anticoagulant medications such as antiplatelet agents, warfarin, and low-molecular-weight heparin (LMWH). These medications may increase the risk of bleeding complications.
- Heparin administration should be delayed for 1 hour after block placement.
- Epidural catheters may be removed 2 to 4 or more hours after the last heparin dose and once laboratory coagulation values have been evaluated and are normalized.
- Bloody or difficult block placement may increase the risk of epidural hematoma formation in the setting of intraoperative anticoagulation; however, there is insufficient data to warrant canceling a case. Discussion of risks and benefits with the surgeon regarding proceeding is warranted.
- Postoperative care should monitor for signs of hematoma such as motor blockade. Use of weak local anesthetic solutions may facilitate detection.

Preoperative low-molecular-weight heparin

Neuraxial blockade should not be performed if the patient is on other antiplatelet or oral anticoagulant medications in combination with LMWH. This combination increases the risk of spinal and epidural hematoma formation in the setting of neuraxial blockade. In the case of traumatic placement, first dose of LMWH should be at 24 hours postoperatively. LMWH has its peak effect 2 to 4 hours after administration.

- *Prophylactic LMWH*. An example of a prophylactic dose is enoxaparin 40 mg qd or 30 mg q12 hours. Block placement should occur no sooner than 10 to 12 hours after the last dose of LMWH and should be maintained only if single-daily dosing is planned. If LMWH is administered within 2 hours of surgery (prophylactic dose), neuraxial blockade should be avoided.
- *Treatment dose LMWH*. An example of a treatment dose is enoxaparin 1.5 mg per kg qd or 1 mg per kg q12 hours. Block placement should occur no sooner than 24 hours after the last dose of LMWH and only if treatment dosing is being discontinued.

Postoperative low-molecular-weight heparin

- *Prophylactic LMWH, twice-daily dosing*. This dosing regimen may be associated with an increased risk of hematoma. The first dose of LMWH should be administered no sooner than 24 hours postoperatively. Epidural catheters should not be maintained in this situation but may be left in overnight, and should be removed at least 2 hours before the first LMWH dose.
- *Prophylactic LMWH, single-daily dosing*. Epidural catheters may be maintained in this situation, but only after a thorough risk/benefit analysis. The first dose of LMWH should be given 6 to 8 hours postoperatively. The second dose should be given no sooner than 24 hours after the first dose. The epidural catheter should be removed 10 to 12 hours after the last dose of LMWH, and the subsequent dose should be given no sooner than 2 hours after catheter removal.
- *Treatment dose LMWH*. Epidural catheters should not be maintained in this situation. The first dose of LMWH should be given 24 hours after catheter removal.

Oral anticoagulants

- *Aspirin*. There is no contraindication to neuraxial anesthesia in patients taking aspirin alone (81 mg or 325 mg).
- *NSAIDs*. There is no contraindication to neuraxial anesthesia in patients taking NSAIDs alone.
- *Preoperative Coumadin*
  a. Coumadin should be stopped 4 to 5 days before a neuraxial block and the patient should not be on any additional antiplatelet or anticoagulant medications.
  b. The prothrombin time/international normalized ratio (PT/INR) should be measured before the block and should be normalized. Of note, if warfarin is stopped for less than 4 days, INR (determined mainly by factors II and X) may not be reflective of coagulation status (determined mainly by facor VII).
  c. Clinicians' threshold for neuraxial blockade vary. Many suggest an epidural may be placed if the INR is less than or equal to 1.2 and that aspinal may be placed if the INR is less than or equal to 1.3.
  d. For patients receiving an initial preoperative coumadin dose, the PT/INR should be checked before neuraxial block if the first dose was given more than 24 hours earlier or if a second dose has been given.
- *Postoperative Coumadin*
  a. Epidural catheters may be maintained in patients on Coumadin up until the INR is less than 1.5. The PT/INR should be monitored daily and assessed before catheter removal.
  b. Epidural catheters should be removed while the INR is less than 1.5.
  c. If the INR is greater than 1.5, consider discontinuing other medications that may affect coagulation or administration of fresh frozen plasma followed by a repeat coagulation profile prior to epidural catheter removal. These patients should be monitored closely after removal of the catheter for signs of neurologic dysfunction.
- *Preoperative clopidogrel (Plavix) and ticlopidine (Ticlid)*
  a. Plavix must be held for a minimum of 7 days before neuraxial block placement.
  b. Ticlid must be held for a minimum of 14 days before neuraxial block placement.
- *Preoperative abciximab, eptifibatide, and tirofiban*
  a) GPIIb/IIIa inhibitors are profound inhibitors of platelet aggregation. Consider confirming platelet function prior to neuraxial block.
  b) Abciximab must be held for a minimum of 24 to 48 hours prior to neuraxial blockade.
  c) Eptifibatide and tirofiban must be held 4 to 8 hours prior to block placement.

Dehring DJ, Arens JF. Pulmonary thromboembolism: disease recognition and patient management. *Anesthesiology*. 1990;73:146–164.

Horlocker TT, Wedel DJ, Rowlingson JC, et al. Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy: American Society of Regional Anesthesia and Pain Medicine evidence-based guidelines (3rd Edition). *Reg Anesth Pain Med.* 2010;35(1):64–101.

Liu SS, Mulroy MF. Neuraxial anesthesia and analgesia in the presence of standard heparin. *Reg Anesth Pain Med.* 1998;23(6 suppl 2):157–163.

B. Chronic Opioid Therapy and Perioperative Pain Management

B.1. How does chronic opioid therapy influence postoperative pain management?

In recent years, a greater emphasis has been placed on pain as an important health problem, with The Joint Commission even labeling pain as the "fifth vital sign." Consequently, opioids now play a greater role in the treatment of chronic pain of various causes. This has resulted in a rapid increase in the consumption of opioid analgesics. For example, between 1999 and 2003, the annual sales of outpatient opioid analgesics in the United States increased by approximately 130%, more than doubling the sales recorded in the previous decade. Because more patients are treated chronically with opioids, every anesthesiologist is likely to be confronted with acute pain management issues in these patients. Chronic opioid-consuming patients can experience significant postoperative pain given that healthcare professionals are not accustomed to their markedly increased opioid requirements.

Patients on long-term opioid therapy are more likely to require surgery and higher doses of opioids postoperatively. Although the prevalence of chronic opioid-consuming patients who present for surgery is not described, the growing use of opioids is likely to increase the number of such patients. Patients with chronic pain are more likely to have high levels of postoperative pain, and increased postoperative pain has been associated with an increased risk of chronic postsurgical pain. Therefore, the aggressive treatment of postoperative pain is important for patients with chronic pain because they represent a population that is particularly vulnerable to develop chronic postsurgical pain.

Although available data are limited, the management of postoperative pain seems to be more difficult in chronic opioid-consuming patients even when they consume only a modest daily opioid dose. Tolerance to any one opioid preparation results in a clinically measurable increased tolerance to most others.

Carroll IA, Angst MS, Clark JD. Management of perioperative pain in patients chronically consuming opioids. *Reg Anesth Pain Med.* 2004;29:576–591.

Mehta V, Langford RM. Acute pain management for opioid dependent patients. *Anaesthesia.* 2006;61:269–276.

Mitra S, Sinatra RS. Perioperative management of acute pain in the opioid-dependent patient. *Anesthesiology.* 2004;101:212–227.

Rapp SE, Ready LB, Nessly ML. Acute pain management in patients with prior opioid consumption: a case controlled retrospective review. *Pain.* 1995;61:195–201.

Swenson JD, Davis JJ, Johnson KB. Postoperative care of the chronic opioid-consuming patient. *Anesthesiol Clin North America.* 2005;23:37–48.

B.2. What are the causes for increased postoperative pain and opioid consumption in patients chronically using opioids?

Chronic exposure to opioids may result in a need to increase the dose over time to maintain the desired analgesic effect. The need for escalating the dose is often

attributed to the development of tolerance. However, dose escalation can be the result of other factors, such as the progression of the underlying disease.

Recent evidence points to opioid-induced hyperalgesia as an alternative neuropharmacologic phenomenon to explain the need to escalate the opioid dose over time. Paradoxically, administration of opioids may induce an increased sensitivity to pain (hyperalgesia). Further complicating matters, the phenomena of tolerance and hyperalgesia can coexist.

Clinical surveys of long-term opioid use in patients with both cancer and non–malignancy-associated pain have not shown escalating drug dosage to be inevitable; however, some degree of dose increase over time is often observed, particularly in younger patients and with use of short-acting opioids.

Carroll IA, Angst MS, Clark JD. Management of perioperative pain in patients chronically consuming opioids. *Reg Anesth Pain Med*. 2004;29:576–591.

Mitra S, Sinatra RS. Perioperative management of acute pain in the opioid-dependent patient. *Anesthesiology*. 2004;101:212–227.

B.3. What are the main differences between a chronic opioid-consuming patient and a patient who abuses or is addicted to opioids?

Patients undergoing surgery may not admit that they are actively abusing pain medications; however, difficulties in achieving adequate postoperative pain control may provide a hint to such abuse.

Many of the issues with respect to chronic opioid-consuming patients also apply to patients who abuse or are addicted to opioids. However, several important differences exist. First, the daily dose of opioid consumed by opioid-abusing patients before surgery is typically larger. Second, opioid-abusing or opioid-addicted patients often suffer from coexisting psychiatric diseases. For example, heroin addicts have an elevated prevalence of depression, anxiety, psychosis, and personality disorders. Depression and anxiety are independent predictors of severe pain after surgery and may complicate the management of postoperative pain. Third, the attitude of healthcare providers toward the use of opioids for controlling pain may be influenced by the abuse history, which makes these patients particularly vulnerable to inadequate postoperative pain control.

De Moja CA. Longitudinal survey of anxiety and depression in drug users and addicts. *Psychol Rep*. 1992;70(3 pt 1):738.

Von Limbeek J, Wouters L, Kaplan CD, et al. Prevalence of psychopathology in drug-addicted Dutch. *J Subst Abuse Treat*. 1992;9:43–52.

B.4. What issues need to be considered in the opioid-tolerant patient who is scheduled for surgery?

Tolerance develops at different rates to desired (analgesia) and undesired effects (sedation, nausea, euphoria, respiratory depression, constipation). Long-term use of opioids results in tolerance to some opioid effects such as analgesia, nausea, sedation, and respiratory depression but not to miosis or constipation. Cross-tolerance with other opioids also occurs. Opioid-tolerant patients report higher pain scores at rest and on movement and also remain longer under the care of acute pain services (APSs) than do other patients. The incidence of opioid-induced nausea and vomiting, however, may be lower in opioid-tolerant patients.

de Leon-Casasola OA, Myers DP, Donaparthi S, et al. A comparison of postoperative epidural analgesia between patients with chronic cancer taking high doses of oral opioids versus opioid-naïve patients. *Anesth Analg*. 1993;76:302–307.

Jage J, Bey T. Postoperative analgesia in patients with substance use disorders: part I. *Acute Pain*. 2000;3:141–156.

Rapp SE, Ready BL, Nessly ML. Acute pain management in paients with prior opioid consumption: a case-controlled retrospective review. *Pain*. 1995;61:195–201.

B.5. What would be your strategy regarding preoperative information and choice of anesthesia technique?

Acute pain management in opioid-dependent patients is a complex issue. There is a tendency among providers to use opioids sparingly, resulting in both poor pain management and withdrawal phenomena. As a result, patients may react with a degree of suspicion, mistrust, or even hostility. Patients need to be reassured that their drug history and dependence will not be an obstacle to the relief of pain. During assessment, care should be exercised to maintain privacy and confidentiality.

Despite the increasing prevalence of opioid dependency, there are few controlled studies available to guide the anesthesiologist in optimizing anesthetic and analgesic care. Because the minimum daily opioid dose that significantly increases postoperative opioid requirements and pain is not known, all patients on chronic opioids should be informed about the potential for severe pain and increased opioid requirements during the postoperative period. Patients should be informed about alternative analgesic techniques that complement opioids.

The selection of anesthesia technique has to be done on an individual basis because there are no data available favoring general, regional, or combined anesthesia for this specific patient population. Although there is no evidence indicating superiority of regional anesthesia for chronic pain patients, individual consideration is likely to favor regional anesthesia. Expert opinion suggests that opioid-tolerant patients should be offered regional anesthesia or analgesia, particularly for procedures performed on the extremities. Advantages of a regional anesthetic and analgesic approach include reduction in opioid requirements and improvement in distal perfusion as a result of sympathetic blockade.

Iocolano CF. Perioperative pain management in the chemically dependent patient. *J Perianesth Nurs*. 2000;15:329–347.

Kopf A, Banzhaf A, Stein C. Perioperative management of the chronic pain patient. *Best Pract Res Clin Anaesthesiol*. 2005;19:59–76.

B.6. What are the choices for perioperative pain management in opioid-tolerant patients?

Management of these patients should focus on two main goals: (1) effective analgesia and (2) prevention of withdrawal. Pre-existing opioid medications must be continued throughout the perioperative period to provide baseline analgesia and to avoid withdrawal. This applies for general anesthesia as well as regional anesthesia. During surgery, the required opioid dose consists of the daily opioid dose taken before surgery and the opioid dose necessary for the surgical intervention. The use of a continuous infusion of opioid may be the best way to provide a steady serum concentration if the oral route is unavailable perioperatively.

Catching up on the opioid dose in the postoperative period can be difficult because of inevitable delays in obtaining and administering opioids at the bedside, the high levels of pain that patients may experience, and a possible reluctance of recovery room staff to administer a sufficiently large opioid dose. Requirements for individual patients are difficult to predict; however, patients who use even modest opioid doses (<50 mg/day oral morphine equivalent) before surgery may often require their baseline opioid dose plus two or more times the amount of opioids typically used for adequate pain control in opioid-naive patients.

Regional anesthesia techniques have many benefits and may be particularly useful in chronic opioid-consuming patients because they provide excellent analgesia to patients prone to severe postoperative pain experiences and avoid the need for high-dose opioids. Neuraxial opioids have also been used effectively in opioid-tolerant patients, and although higher doses are often required, these generally do not result in an increase in adverse effects.

Nevertheless, chronic opioid-consuming patients treated with regional and neuraxial techniques for postoperative pain control should also have access to systemic opioids by the intravenous or oral route for prevention of opioid withdrawal. IV-PCA is a useful modality for pain relief in opioid-tolerant patients, provided that pain intensity and opioid consumption are monitored and background requirements are provided if the patient cannot take their usual opioid. Larger bolus doses will often be needed. Opioid rotation (i.e., using an opioid that is different from their preadmission opioid) may also be of use.

Withdrawal from opioids should be prevented by maintenance of normal preadmission opioid regimens where possible, or appropriate substitutions with another opioid or the same opioid through another route. It may be of benefit to check preadmission opioid doses with the patient's doctor or pharmacist. The use of unauthorized additional opioids (licit or illicit) or diversion may affect both pain relief and the risk of adverse effects.

Ketamine can reduce opioid requirements in opioid-tolerant patients, both intraoperatively and postoperatively. It is an N-methyl-D-aspartic acid receptor antagonist and results in analgesia by inhibiting the processing of nociceptive information. Evidence shows that the addition of N-methyl-D-aspartic acid receptor antagonists with other analgesics or as a sole agent for chronic (e.g., complex regional pain syndrome), ischemic, or neuropathic pain states can reduce the requirement for other analgesic agents. When ketamine is used as a continuous infusion in the postoperative setting, it can have an opioid-sparing effect, although there is no reduction in opioid-related side effects. It can also serve as a bridge until the patient is able to tolerate their home oral regimen. Perioperatively, ketamine is best used as an adjunct to opioid medications.

Multimodal analgesic regimens including combinations of NSAIDs, acetaminophen, gabapentin, and topical local anesthetics are likely to provide benefit as well. Opioid antagonists (naloxone, naltrexone) or mixed agonist–antagonists (e.g., buprenorphine, pentazocine) should be avoided because their use precipitates acute withdrawal reactions.

Australian and New Zealand College of Anaesthetists and Faculty of Pain Medicine. The opioid tolerant patient. In: *Acute Pain Management: Scientific Evidence*. Melbourne, Australia: Australian and New Zealand College of Anaesthetists and Faculty of Pain Medicine; 2005.

de Leon-Casasola OA, Lema MJ. Epidural bupivacaine/sufentanil therapy for postoperative pain control in patients tolerant to opioid and unresponsive to epidural bupivacaine/morphine. *Anesthesiology*. 1993;80:302–307.

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B.7. What issues need to be considered before discharging an opioid-tolerant patient?

Discharge planning must take into account the potential for prescribed opioids to be abused or misused. Appropriate use of nonopioid analgesics where possible, communication with the primary physician, and patient education and support must all be considered.

Chronic opioid-consuming patients typically require significantly higher postoperative opioid doses for adequate pain control than they received before surgery for their chronic pain symptoms. Attempting to discharge chronic opioid-consuming patients on the same opioid regimen they adhered to before surgery often results in inadequate pain control. Whatever the final oral dose chronic opioid-consuming patients are stabilized on at discharge, a slow tapering from this dose toward the preoperative opioid dose over 2 to 4 weeks is often a reasonable goal. In the case under consideration, the transdermal fentanyl patch should be left in place to provide the patient's pre-existing opioid requirement, and additional short-acting analgesics should be prescribed for postoperative pain.

C. Perioperative Pain Management for Ambulatory Surgery

C.1. What would be your preoperative considerations and advice to the patient?

Adequate postoperative pain management is often the limiting factor when determining whether a patient can have surgery performed as an ambulatory surgical procedure. Ensuring that the patient has appropriate expectations of the outcome of laparoscopic cholecystectomy is critical for a successful conclusion to the procedure, especially with regard to postoperative pain. Unrealistic expectations for no pain at all can be met with anger, disappointment, and the fear and anxiety that something has gone wrong. Failure to meet unrealistic expectations can even lead to litigation.

Planning for postoperative pain management should begin in the preoperative period. Patient education regarding the degree of pain that might be expected and discussion of the pain assessment tools and modalities of pain treatment that might be utilized should reduce the patient's anxiety and the fear of unrelieved pain. Reduced patient anxiety has been shown to reduce the incidence and severity of postoperative pain. In addition, patients have to be made aware of the importance of communicating their analgesic needs. Patients should receive instruction on the importance of coughing, deep breathing, ambulation, and postoperative rehabilitation. Patient information on acute postoperative pain management is available from public sources and patients can be directed to these sources for self-study.

Details of the complications of laparoscopic cholecystectomy given to patients vary between countries and cultures. The most relevant for postoperative pain is to mention the risk of conversion to open laparotomy in a small percentage of cases, which will be associated with a significantly larger incision, more pain, and longer period of hospitalization. Patients need to be informed that there are three types of pain often associated with laparoscopic cholecystectomy: (1) incisional, (2) visceral, and (3) shoulder pain. It is helpful to describe, in particular, the high incidence of referred pain in the shoulders and to reassure the patient that this is related to the laparoscopy and not necessarily their heart or chest. The patient should be informed that there is a relatively high risk of postoperative nausea and vomiting after laparoscopic cholecystectomy (~30% to 50%) and that appropriate prophylaxis will be administered (antiemetic strategies can be tailored based on clinical risk scores for nausea and vomiting).

Predischarge patient information should also include the following: (1) that patients will receive analgesic and/or antiemetic medications (or prescriptions, or both) for management of pain and postoperative nausea and vomiting at home, (2) that the hospital (surgeon or nurse) will make a follow-up call and schedule a follow-up appointment and, (3) that they will get contact telephone numbers in case there are problems or questions.

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C.2. What are the consequences of inadequate pain management after ambulatory surgery?

In the ambulatory setting, the type of surgery is a significant predictor of severity of postoperative pain. Even when postoperative pain is effectively treated in the postanesthesia care unit, it often recurs once the patient has returned home. A common example is a peripheral nerve block for orthopedic surgery, which provides excellent analgesia until the block has worn off several hours later. Indeed, Rawal et al. reported that 30% to 35% of patients undergoing ambulatory surgery experienced moderate to severe pain at home.

Uncontrolled pain is associated with an increased incidence of postoperative nausea, agitation, prolonged postanesthesia care unit stay, delayed discharge from an ambulatory facility, and unanticipated hospital admission. Inadequate postoperative pain control is also the most frequent reason for patients to contact their family practitioner after discharge from the hospital. Importantly, the presence of postoperative symptoms including pain contributes to patient dissatisfaction with their surgical experience (see Table 50.1).

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Table 50.1 Consequences of Inadequate Pain Management after Ambulatory Surgery

Increased postanesthesia care unit stay
Increased phase II unit stay
Delayed discharge at home
Unanticipated hospital admission
Increased contact with family practitioner
Delayed return to daily living function
Decreased patient satisfaction

C.3. What is the role of premedication or preoperative analgesic?

Preoperative administration of opioid or nonopioid analgesics reduces analgesic requirements and pain scores in the immediate postoperative period. However, opioid premedication is controversial in the ambulatory setting because it may increase the incidence of opioid-related side effects and even delay recovery. Premedication with oral NSAIDs given 60 to 90 minutes before surgery can avoid these concerns and reduce the degree of postoperative pain, analgesic requirements, and time to discharge.

Pre-emptive analgesia refers to the concept that an analgesic medication or intervention administered before surgical tissue injury may produce a greater effect than the same medication or intervention administered following surgical tissue injury. This pre-emptive analgesic effect has been demonstrated for several different medications in animal models, but clinical studies do not support a significant role for pre-emptive analgesia in human patients.

For laparoscopic cholecystectomy, there is no strong evidence that preincisional timing of analgesic administration (pre-emptive analgesia) decreases the intensity or duration of postoperative pain, when compared with intraoperative or postoperative administration. A systematic review (Møiniche et al., 2002) confirms that there is no overall clinical benefit of preoperative analgesia on postoperative pain in a large number of studies examining a variety of analgesic techniques in different surgical procedures.

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Møiniche S, Kehlet H, Dahl JB. A qualitative and quantitative systematic review of preemptive analgesia for postoperative pain relief: the role of timing of analgesia. *Anesthesiology*. 2002;96:725–741.

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Woolf CJ, Chong MS. Preemptive analgesia—treating postoperative pain by preventing the establishment of central sensitization. *Anesth Analg*. 1993;77:362–379.

C.4. Does the choice of anesthetic technique influence postoperative pain?

The choice of anesthetic technique has been shown to have a significant influence on postoperative analgesia in patients undergoing ambulatory surgery. Regional anesthesia techniques offer a number of advantages in outpatient surgery, including prolonged postoperative analgesia.

Opioids remain the primary drugs used to provide intraoperative analgesia. As a result of the faster recovery from ultrashort-acting opioids such as remifentanil, it is necessary to administer longer-acting opioid or nonopioid analgesics to achieve adequate postoperative pain control. However, the role of opioids in ambulatory surgery remains controversial. The use of opioids may be associated with a dose-dependent increase in adverse effects, including nausea, vomiting, sedation, bladder dysfunction, and respiratory depression, all of which may contribute to a delayed recovery.

Only one peer-reviewed study has, to date, prospectively examined the effect of a neuraxial technique on postoperative pain management in patients for laparoscopic cholecystectomy. This study examined combined epidural and general anesthesia (CEGA) versus total intravenous anesthesia (TIVA) and showed a reduction in postoperative pain scores for CEGA versus TIVA. However, an epidural technique is not recommended for routine anesthetic management in patients undergoing laparoscopic cholecystectomy because the majority of patients do not convert to open procedures

and thus the incisions are small and minimally painful. Nevertheless, in certain high-risk pulmonary patients, CEGA can be justified.

TIVA offers an alternative to inhalational anesthesia, and although rapid recovery from anesthesia and reduction in nausea and vomiting are recognized benefits, the analgesic components of TIVA have a very short duration and do not contribute to improved postoperative analgesia.

There is enough evidence in the literature to support the use of incisional local anesthetic infiltration at end of surgery. Infiltration of the surgical wound with local anesthetic can provide excellent analgesia that outlasts the duration of action of the local anesthetics themselves. Another simple and effective method of reducing the intensity of postlaparoscopic pain is intraperitoneal instillation of local anesthetic. Evidence suggests significant pain relief after laparoscopic cholecystectomy when 15 to 20 mL of 0.5% bupivacaine is administered into the hepato-diaphragmatic space.

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C.5. Are nonsteroidal anti-inflammatory drugs (NSAIDs) effective? If so, does the choice of drug matter?

The opioid-sparing effects of NSAIDs lower the risk of postoperative nausea and vomiting, pruritus, constipation, and respiratory depression, thereby improving patient comfort and allowing for an earlier discharge.

The introduction of a parenteral preparation of NSAID and the widespread acceptance of the concept of multimodal "balanced" analgesia has increased the popularity of NSAIDs in the management of perioperative pain. NSAIDs available for intravenous use include ketorolac, diclofenac, indomethacin, ketoprofen, tenoxicam, and lornoxicam.

However, NSAIDs have weaker analgesic properties than opioids or local anesthetics and also exhibit a "ceiling effect" with respect to their maximum analgesic

effect. Despite their limitations, NSAIDs may decrease the risk of breakthrough pain because of their more prolonged duration of action and are valuable adjuvants when used in combination with opioids and local anesthetics.

There is no documented evidence of superiority of any particular NSAID for perioperative use. Therefore, the choice of NSAID is dependent upon the route of administration, the duration of the analgesia, propensity for side effects, and the cost.

The oral availability of most NSAIDs is high, whereas that after rectal administration, it is low; therefore NSAIDs should be preferably administered orally. Overall, NSAIDs appear to be safe and well tolerated in patients undergoing ambulatory surgery.

COX-2 inhibitors have been demonstrated in multiple clinical trials to produce analgesic efficacy equal to that of the traditional nonselective NSAIDs without the COX-1 mediated adverse effects of inhibition of platelet aggregation or gastroduodenal ulceration. COX-2 inhibitors used over a short period for postoperative analgesia have not been demonstrated to cause any major adverse events in healthy patients.

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C.6. There are three types of pain after laparoscopic cholecystectomy: incisional, subphrenic, and shoulder pain. What is the role of surgical technique in influencing postoperative pain?

The pain after laparoscopic procedures is primarily visceral in origin. Factors responsible for this pain may be related to surgical incisions, carbon dioxide insufflation, and the intra-abdominal pressures maintained during the laparoscopic procedure. Higher insufflation pressures should be avoided, because they can significantly increase the severity of postoperative pain. Subphrenic and shoulder pain after laparoscopic procedures appear to arise from diaphragmatic and phrenic nerve irritation due to insufflated carbon dioxide. This pain tends to be aggravated by ambulation and may persist for several days after surgery. Residual insufflating gas can also increase the intensity of postlaparoscopic pain. Therefore, the abdomen should be actively deflated at the end of the laparoscopic procedure.

Evidence from prospective studies to prevent postoperative pain after laparoscopy includes the following findings:

- Low pressure CO_2 pneumoperitoneum is superior to conventional CO_2 pneumoperitoneum in three out of three controlled studies.
- There is insufficient data to recommend warmed CO_2 pneumoperitoneum for reducing postoperative pain.

- Peritoneal lavage after CO_2 pneumoperitoneum is effective in reducing postoperative pain.
- Helium pneumoperitoneum has no advantage versus CO_2 pneumoperitoneum.

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C.7. What would be your strategy for pain control after discharge home?

After discharge, acetaminophen, NSAIDs, or opioids, either alone or in combination, are frequently used to provide postoperative pain relief.

Given that acetaminophen has a similar efficacy and a better side effect profile than NSAIDs, it should be considered as an alternative to NSAIDs. Coadministration of acetaminophen and NSAIDs has also been advocated.

Codeine and its derivatives are the most commonly used oral opioid analgesics after ambulatory surgery; however, codeine is a prodrug that must be metabolized to its active form codeine-6-glucuronide and there is a documented large amount of inter-individual variability in codeine metabolism, with 9% of Caucasians complete non-metabolizers. Oxycodone and hydrocodone are orally active derivatives of codeine with higher analgesic potency. Controlled-release preparations of oxycodone have longer duration of action and fewer side effects than the older formulations and have been shown to be highly effective postoperatively. However, there is concern over the misuse of time-release oxycodone in the Oxycontin formulation. The tablet is a nondigestible matrix that is filled with large amounts of oxycodone that are slowly time-released by diffusion out of the matrix. If the matrix is crushed or cut and ingested, the entire drug contained in the preparation is immediately released, which has led to abuse and also to a number of deaths due to accidental overdose. Providers should exercise caution when prescribing this medication. Generally, because postsurgical pain is acute rather than chronic in nature, short-acting opioids for breakthrough pain are sufficient.

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D. The Role of an Acute Pain Service

D.1. What is the extent of the problem and which patients are at greatest risk of undertreatment?

Pain relief after surgery continues to be a major medical challenge. Despite a significant improvement over the last decade in our understanding of acute and chronic pain mechanisms and the establishment of APSs, recent studies continue to report that postoperative pain management is not satisfactory for many patients. In addition, publications of guidelines for acute pain management, the introduction of pain as "the fifth vital sign," and the incorporation of the standards advocated by The Joint Commission have not yet translated into improved postoperative analgesia.

More than 30% of patients report moderate to severe pain after surgery. More recent surveys of postdischarge pain put that number even higher. Clinical risk scores to identify patients most at risk for postoperative pain are scarce and not commonly used in practice. Certain patient subpopulations are at greater risk of undertreatment, including infants and children, the elderly, ethnic minorities, and patients with psychiatric illness or those unable to communicate.

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D.2. What are the consequences of inadequate postoperative pain relief?

Evidence suggests that inadequate relief of postoperative pain results in harmful physiologic and psychological consequences that lead to significant morbidity, delaying recovery and the return to activities of daily living. Postoperative splinting can lead to atelectasis, and autonomic overactivity associated with pain can result in increased myocardial oxygen demand and increased incidence of perioperative myocardial infarction in at-risk adults. In children, postoperative pain has been found to be an important cause for long-lasting temper tantrums and behavioral changes. In addition, the presence of postoperative pain significantly contributes to patients' dissatisfaction with their anesthesia and surgical experience.

Chronic pain after surgery, also referred to as persistent postsurgical pain, has long been recognized as a major factor in delaying recovery and return to normal daily living. Long-lasting pain is often reported after several common surgical procedures including thoracotomy, mastectomy, hernia repair, and limb amputation. Predisposing risk factors include the severity of preoperative and postoperative pain, intraoperative nerve injury, and psychological vulnerability. Specific early analgesic interventions may reduce the incidence.

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D.3. What is the role of an acute pain service (APS) in improving postoperative pain management?

The immediate solution to the problem of inadequate pain relief lies not so much in the development of new analgesic drugs or technologies but in the development of an appropriate organization to utilize existing expertise effectively.

Moreover, effective acute pain management results from education and organizational structure for the delivery of pain relief rather than the specific analgesic techniques themselves. Even simple methods of pain relief can be more effective if proper attention is given to their appropriate, evidence-based use. In many institutions, APSs assume responsibility for managing more advanced methods of pain relief such as patient-controlled analgesia, epidural analgesia, and peripheral nerve catheters to ensure patients receive optimum care from providers well-versed with these analgesic modalities. Additionally, APSs often follow chronic pain patients who are difficult for primary teams to manage and whose complex pain issues are best treated using a multimodal approach.

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D.4. Does an APS improve postoperative outcome?

The introduction of APSs has led to an increase in the appropriate use of specialized analgesic techniques, such as IV-PCA, neuraxial blockade, and peripheral nerve catheters. The implementation of these techniques is an advance in improving analgesia and patient well-being and in reducing postoperative morbidity. In addition, an APS may reduce "analgesic gaps" that can occur during the transition from IV-PCA or epidural analgesia to oral analgesic therapy. Although evaluating the safety of analgesic techniques is an important objective of an APS, its role in preventing and reducing

adverse events has not been well-documented; however, consolidation of decisions regarding pain regimens under one service is likely to have several benefits. First, standardization of protocols decreases prescription or drug administration error. Second, having one service responsible for pain orders decreases the incidence of redundancy and multiple opioid orders. And finally, the availability of a service primarily dedicated to pain is likely to increase the efficacy of interventions and decrease patient pain scores.

In a recent literature review, Werner et al. evaluated the effects of an APS on postoperative outcome in 44 retrospective and 4 prospective clinical trials including 84,097 postoperative patients. The authors found that the implementation of an APS was associated with a significant decrease in pain intensity. In addition, the introduction of an APS was associated with less postoperative nausea and vomiting and urinary retention. However, the authors could not draw clear conclusions about patient satisfaction or postoperative morbidity due to a large variability in the studies regarding composition of the APSs and services provided.

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CHAPTER 51

Acupuncture

YUAN-CHI LIN

A 66-YEAR-OLD WOMAN

was scheduled for arthroscopic surgery of her right knee. She experienced severe postoperative nausea and vomiting in the postanesthesia care unit. Despite the use of conventional therapies, her nausea and vomiting persisted. Her past medical history was significant for mastectomy for breast cancer, headache, chronic neck and back pain, osteoarthritis in her knees, peptic ulcer disease, and allergy to Novocain. What role can acupuncture therapy play in her care?

A. Acupuncture as a Complementary Medical Therapy

1. What is acupuncture?
2. How is acupuncture practiced?
3. What are the mechanisms of acupuncture analgesia?
4. What were the conclusions of the National Institutes of Health Consensus Conference about acupuncture?

B. Acupuncture for the Treatment of Chronic Conditions

1. Can acupuncture be used for the treatment of postoperative nausea and vomiting?
2. Can acupuncture be used for the treatment of chemotherapy-induced nausea and vomiting?
3. How effective is acupuncture for the management of chronic headache?
4. Can acupuncture be used for the treatment of chronic neck and back pain?
5. Can acupuncture be used for the treatment of osteoarthritis?
6. What role can acupuncture play in the care of patients with cancer?

C. Complications

1. What are the complications of acupuncture treatment?

A. Acupuncture as a Complementary Medical Therapy

A.1. What is acupuncture?

The word *acupuncture* is derived from the Latin words *acus*, "needle," and *punctura*, "a pricking." The original Chinese term for acupuncture is *Jin Jiao*, which describes the practice of "acupuncture and moxibustion." Moxibustion, which is the burning of moxa (*Artemisia vulgaris*) over the acupuncture points, can also be used for the treatment of various illnesses.

Acupuncture is one of the treatment modalities of comprehensive traditional Chinese medicine. The history of traditional Chinese medicine can be traced back 3000 years. The *Yellow Emperor's Classic of Internal Medicine* from the fourth century BC described the practice of puncturing the body for pain relief. Traditional Chinese medicine is a system of thoughts and practices that are based on the investigations of nature, causes, and effects. It takes the principles of realism and ethics and employs them for the prevention and healing of illnesses.

The theory of *yin and yang* underlies the theoretical framework of acupuncture. Yin and yang are two opposite dynamics that cannot exist in isolation. Rather, they are in a constant state of dynamic balance. If yin and yang are not balanced, illnesses may occur in the body.

The human body is controlled by a vital force called *Qi*. Qi circulates throughout the body and defends its various parts. There are 365 identified acupuncture points in the body, which fall along 12 principal and eight extrameridian systems. Qi was postulated to flow through these meridians in the body.

A.2. How is acupuncture practiced?

Acupuncture utilizes a technique of inserting very fine needles into strategic points in the body called *acupuncture points*. Acupuncture needles vary from 0.5 to 5 inches. in length and from 36 to 42 gauge. There are a wide variety of needles currently available. In *Huang Di Nei Jin* (*The Yellow Emperor's Internal Classic*), Ling Shu described nine shapes of acupuncture needles. Sterile, disposable stainless steel acupuncture needles are the current standard for acupuncture treatment.

After sterilizing the site of the needle entrance on the skin, the acupuncture needle is inserted few millimeters into the epidermis. Following placement of the acupuncture needle, stimulation of the acupuncture point may be achieved manually or by the use of low-voltage electrodes introduced to the needle in a method called *electroacupuncture*.

Each acupuncture point has a prescribed depth of insertion. Manual techniques may involve the lifting and thrusting of the needle or twisting and twirling. *De-Qi* is a typical sensation that is associated with proper acupuncture needle position. Patients describe the sensation as a feeling of soreness, numbness, warmth, heaviness, or pressure around the area where the needle is inserted. The De-Qi sensation is mediated through nonmyelinated C fibers. Many practitioners consider this sensation to be crucial in achieving the effects of acupuncture. Electroacupuncture achieves a similar effect through the use of high- or low-frequency electricity.

Very little pain is associated with the introduction of acupuncture. For various conditions, multiple acupuncture treatment sessions over an extended period may be required to achieve its greatest effectiveness.

Auricular, hand, and scalp acupuncture can be used as microsystems of acupuncture. For example, for the auricular acupuncture (Fig. 51.1) the upper region of the external ear is used to alleviate conditions in the leg and feet. The middle region of the external ear represents chest and back pain. The lower regions are used to relieve headache and neurologic conditions. Auricular acupuncture can also be used for preoperative anxiety control.



Figure 51.1 Auricular acupuncture.
Δ, heart point ; •, shen men; ◆, autonomic point.

The frequency, as well as the number of acupuncture treatments, varies among acupuncture providers. Most practitioners would agree that more than one treatment is necessary to experience the full effect of acupuncture.

Chernyak GV, Sessler DI. Perioperative acupuncture and related techniques. *Anesthesiology*. 2005;102:1031–1049.

A.3. What are the mechanisms of acupuncture analgesia?

Acupuncture inhibits the transmission of pain according to the gate control theory. It may act by stimulating sensory A-β fibers, thereby directly inhibiting the spinal transmission of pain by a smaller A-δ and C fibers.

Acupuncture stimulates the production of endogenous opioid peptides, such as endorphins, enkephalins, and stimulation of the endogenous descending inhibitory pathways. In human studies, analysis of cerebrospinal fluid showed elevated levels of serotonin, endorphins, and enkephalins following acupuncture treatments. Acupuncture analgesia is mainly achieved by the activation of the endogenous antinociceptive system to modulate pain transmission and pain response. Low-frequency (2 Hz) and high-frequency (100 Hz) electrical acupuncture selectively induces the release of enkephalins and dynorphins in both experimental animals and humans. Acupuncture analgesia may be reversed by naloxone.

Functional magnetic resonance imaging has been used to investigate the effect of acupuncture in normal volunteers. Acupuncture needle manipulation on the

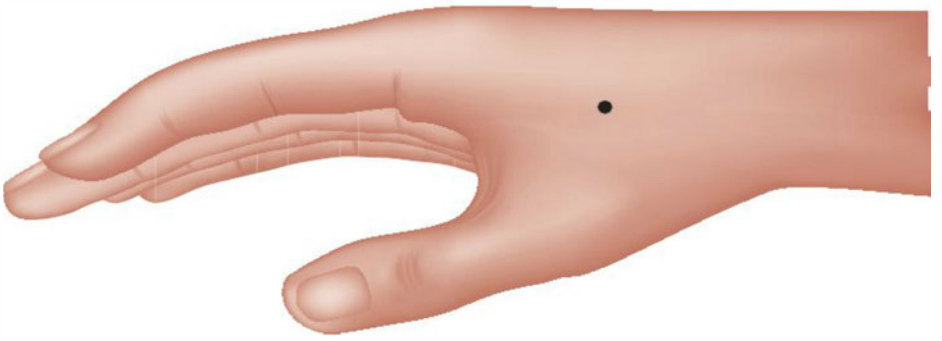

Figure 51.2 LI 4 (Hegu) acupuncture point is on the dorsum of the hand, between the first and second metacarpal bones, radial to the midpoint of the second metacarpal bone.

LI 4 (Hegu) point (Fig. 51.2) modulates the activity of the limbic system and subcortical structure revealed in functional magnetic resonance imaging. Individual variation occurs in the cortical activation patterns elicited by electrical acupuncture stimulation. Real acupuncture elicited significantly higher activation than sham acupuncture over the hypothalamus and primary somatosensorimotor cortex and deactivation over the rostral segment of anterior cingulated cortex.

Abraham MK, Menon SS, Bindumole PS. Thoracoscopic repair of eventration of diaphragm. *Indian Pediatr*. 2003;40:1088–1089.

He L. Involvement of endogenous opioid peptides in acupuncture analgesia. *Pain*. 1987; 31:99–121.

Hui K, Liu J, Makris N, et al. Acupuncture modulates the limbic system and subcortical gray structures of the human brain: evidence from fMRI studies in normal subjects. *Hum Brain Mapp*. 2000;9:13–25.

Ulett G, Han S, Han J. Electroacupuncture: mechanisms and clinical application. *Biol Psychiatry*. 1998;44:129–138.

Wu M, Sheen J, Chuang K, et al. Neuronal specificity of acupuncture response: a fMRI study with electroacupuncture. *Neuroimage*. 2002;16:1028–1037.

A.4. What were the conclusions of the National Institutes of Health Consensus Conference about acupuncture?

A National Institutes of Health Consensus Conference concluded that acupuncture is an effective therapeutic intervention that is widely practiced in the United States. Promising results have emerged, for example, supporting the efficacy of acupuncture in adult postoperative and chemotherapy-related nausea and vomiting and in postoperative dental pain. In other conditions, such as addiction, stroke rehabilitation, headache, menstrual cramps, tennis elbow, fibromyalgia, myofascial pain, osteoarthritis, low back pain, carpal tunnel syndrome, and asthma, acupuncture may also be useful as an adjunct treatment, as an acceptable alternative, or when included in a comprehensive management program. Further research is expected to uncover additional areas in which acupuncture interventions will be useful.

National Institutes of Health Consensus conference. Acupuncture. *JAMA*. 1988;280:1518–1524.

B. Acupuncture for the Treatment of Chronic Conditions

B.1. Can acupuncture be used for the treatment of postoperative nausea and vomiting?

Postoperative nausea and vomiting are frequent occurrences following surgery and are best avoided whenever possible. Acupuncture is a commonly used therapy for the treatment of these symptoms. Stimulation of the acupuncture PC-6 (*Nei Guan acupuncture point*; in Chinese this means *gate of the internal organ*) points by acupuncture needles, electrical apparatus, pressure, or magnets is used to achieve relief of nausea and vomiting. The PC-6 acupuncture point is located 2 cun (tsun), approximately 2.6 inches, above the transverse crease of the wrist, between the tendons of the muscle palmaris longus and muscle flexor carpi radialis (Fig. 51.3).

Studies support the use of acupuncture for the treatment of postoperative nausea and vomiting. A systemic review was conducted of 33 randomized controlled trials of acupuncture and acupressure. The results were positive in 27 of these trials. A randomized controlled trial of pediatric patients undergoing tonsillectomy using electroacupuncture in conscious patients showed significant reduction in the occurrence of nausea compared with those in the sham and control groups. The efficacy of acupuncture for postoperative nausea and vomiting prevention is similar to that commonly used pharmacotherapies. A double-blind, randomized, placebo-controlled study revealed that hand acupressure is an effective method for reducing postoperative vomiting in children after strabismus repair.

PC-6 acupressure is a noninvasive method that may have a place as prophylactic antiemetic therapy during gynecologic surgery. Alkaissi et al. did a prospective randomized controlled trial of acupressure in the prevention of postoperative nausea and vomiting for women undergoing general anesthesia for elective gynecologic surgery, with positive results.

Alkaissi A, Evertsson K, Johnsson VA, et al. P6 acupressure may relieve nausea and vomiting after gynecological surgery: an effectiveness study in 410 women. *Can J Anaesth.* 2002;49:1034–1039.

Rusy LM, Hoffman GM, Weisman SJ. Electroacupuncture prophylaxis of postoperative nausea and vomiting following pediatric tonsillectomy with or without adenoidectomy. *Anesthesiology.* 2002;96:300–305.

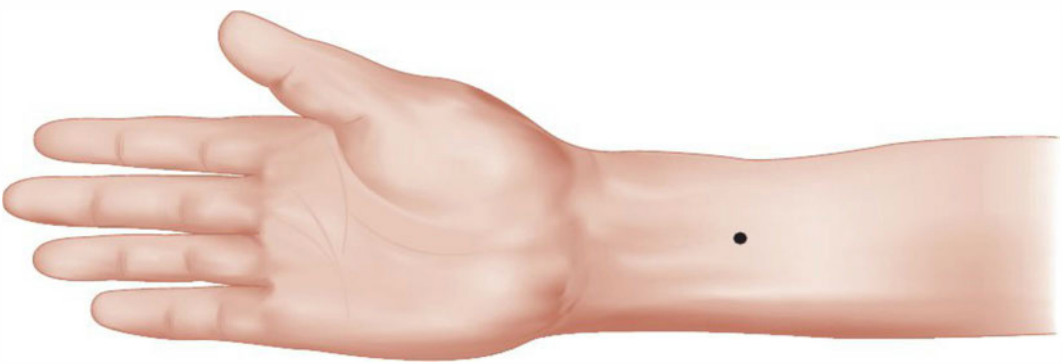

Figure 51.3 The PC-6 acupuncture point is located 2 cun (tsun), approximately 2.6 inches, above the transverse crease of the wrist, between the tendons of the muscle palmaris longus and muscle flexor capri radialis.

Schlager A, Boehler M, Puhringer F. Korean hand acupressure reduces postoperative vomiting in children after strabismus surgery. *Br J Anaesth.* 2000;85:267–270.

Vickers A. Can acupuncture have specific effects on health? A systematic review of acupuncture antiemetic trials. *J R Soc Med.* 1996;89:303–311.

B.2. Can acupuncture be used for the treatment of chemotherapy-induced nausea and vomiting?

Acupressure at the PC-6 acupuncture point has been shown to have a protective effect on people experiencing chemotherapy-induced nausea and vomiting. A review of 11 randomized controlled trials studying the effectiveness of acupuncture point stimulation on chemotherapy-induced nausea and vomiting revealed that electroacupuncture reduced chemotherapy-induced acute vomiting.

Ezzo JM, Richardson MA, Vickers A, et al. Acupuncture-point stimulation for chemotherapy-induced nausea or vomiting. *Cochrane Database Syst Rev.* 2006;(2): CD002285.

B.3. How effective is acupuncture for the management of chronic headache?

Acupuncture therapy for migraine headaches has been reported to be effective in several studies in adults. In a randomized controlled trial of 168 women with migraine, acupuncture was proved to be an adequate migraine prophylaxis. Relative to flunarizine, acupuncture treatment exhibited greater efficiency in the first months of therapy and better patient tolerance. A systemic review of 22 trials including a total of 1,042 patients suggests that acupuncture has a role in the treatment of recurrent headaches. As an added benefit, in a randomized controlled trial of 401 patients with chronic migraine headache, it was also shown that through 12 months of follow-up, acupuncture was relatively cost-effective. Compared with the patients in the control groups, patients receiving acupuncture used 15% less medication, made 25% fewer visits to general practitioners, and took 15% fewer sick days from work.

Cochrane database of systematic reviews of 11 trials with 2,317 participants for patients with episodic or chronic tension-type headache revealed that acupuncture could be a valuable nonpharmacologic tool in patients with frequent episodic or chronic tension-type headaches. In regard to acupuncture for migraine prophylaxis, meta-analysis of 22 trials with 4,419 participants shows acupuncture to be at least as effective as, and possibly more effective than, prophylactic drug treatment and has fewer adverse effects. Acupuncture should be considered a treatment option for patients willing to undergo this treatment.

Allais G, De Lorenzo C, Quirico P, et al. Acupuncture in the prophylactic treatment of migraine without aura: a comparison with flunarizine. *Headache.* 2002;42:855–861.

Dowson D, Lewith GT, Machin D. The effects of acupuncture versus placebo in the treatment of headache. *Pain.* 1985;21:35–42.

Linde K, Allais G, Brinkhaus B, et al. Acupuncture for migraine prophylaxis. *Cochrane Database Syst Rev.* 2009(1):CD001218.

Linde K, Streng A, Jurgens S, et al. Acupuncture for tension-type headache. *Cochrane Database Syst Rev.* 2009(1):CD007587.

Loh L, Nathan PW, Schott GD, et al. Acupuncture versus medical treatment for migraine and muscle tension headaches. *J Neurol Neurosurg Psychiatry.* 1984;47:333–337.

Melchart D, Linde K, Fischer P, et al. Acupuncture for recurrent headaches: a systematic review of randomized controlled trials. *Cephalalgia.* 1999;19:779–786.

Vickers AJ, Rees RW, Zollman CE, et al. Acupuncture for chronic headache in primary care: large, pragmatic, randomised trial. *Br Med J.* 2004;328:744–748.

B.4. Can acupuncture be used for the treatment of chronic neck and back pain?

In a randomized controlled trial of 177 patients with chronic neck pain, the effectiveness of acupuncture, massage, and "sham" laser acupuncture were compared. A study followed 14,161 patients with chronic neck pain for a period of more than 6 months. The patients in the acupuncture group received up to 15 acupuncture sessions over 3 months. The reported neck pain levels and disability scores of the members of the acupuncture group were improved over those of the control group. Treatment success was followed and maintained for 6 months.

A large German clinical study involved 1,162 patients with chronic low back pain indicated that both "real" and "sham" acupuncture treatment were significantly better than conventional therapy for at least 6 months. Another large German study of 1,549 patients with chronic low back pain showed acupuncture plus routine care was associated with marked clinical improvements in patients with chronic low back pain and was relatively cost-effective. A systemic review involve 23 trials of 6,359 patients with low back pain revealed that acupuncture can be a useful supplement to other forms of conventional therapy for nonspecific low back pain.

Haake M, Muller HH, Schade-Brittinger C, et al. German Acupuncture trials (GERAC) for chronic low back pain, randomized, multicenter, blinded, parallel-group trial with 3 groups. *Arch Intern Med.* 2007;167:1892–1898.

Irnich D, Behrens N, Molzen H, et al. Randomised trial of acupuncture compared with conventional massage and "sham" laser acupuncture for treatment of chronic neck pain. *Br Med J.* 2001;322:1574–1577.

Witt CM, Jena S, Brinkhaus B, et al. Acupuncture for patients with chronic neck pain. *Pain.* 2006;125:98–106.

Witt CM, Jenna S, Selim D, et al. Pragmatic randomized trial evaluating the clinical and economic effectiveness of acupuncture for chronic low back pain. *Am J Epidemiol.* 2006;164:487–496.

Yuan J, Purepong N, Kerr DP, et al. Effectiveness of acupuncture for low back pain: a systematic review. *Spine.* 2008;33:887–900.

B.5. Can acupuncture be used for the treatment of osteoarthritis?

Evidence exists for the efficacy of acupuncture for reducing the pain and dysfunction of osteoarthritis. In a study of 300 patients with chronic osteoarthritis of the knee, participants were randomly assigned to acupuncture, minimal acupuncture, or wait list control group. After 8 weeks of treatment, pain and joint function were improved more with acupuncture than with minimal or no acupuncture.

In another randomized controlled trial of 570 patients with osteoarthritis of the knee, the acupuncture group received 23 true acupuncture sessions over 26 weeks. Acupuncture was shown to provide improvement in function and pain relief as an adjunctive therapy for osteoarthritis of the knee when compared with credible sham acupuncture and education control groups.

In a trial of 30 patients with symptomatic osteoarthritis of the knee, participants were randomized into one of three treatment groups. One group of patients received acupuncture alone; another group of patients received acupuncture, but continued on

their symptomatic medication; and the third group of patients used their symptomatic medication for the first 5 weeks and then had a course of acupuncture added. The patients receiving acupuncture were treated twice weekly over 5 weeks. The results of this study concluded that manual and electroacupuncture causes a significant improvement in the symptoms of osteoarthritis of the knee, either alone or as an adjunct therapy, and with no loss of benefit after 1 month.

Berman BM, Lao L, Langenberg P, et al. Effectiveness of acupuncture as adjunctive therapy in osteoarthritis of the knee: a randomized, controlled trial. *Ann Intern Med.* 2004;141:901–910.

Tukmachi E, Jubb R, Dempsey E, et al. The effect of acupuncture on the symptoms of knee osteoarthritis: an open randomised controlled study. *Acupunct Med.* 2004;22:14–22.

Witt C, Brinkhaus B, Jena S, et al. Acupuncture in patients with osteoarthritis of the knee: a randomised trial. *Lancet.* 2005;366:136–143.

B.6. What role can acupuncture play in the care of patients with cancer?

A report of a randomized controlled trial of 90 patients with cancer pain revealed clear benefit from auricular acupuncture for cancer patients experiencing pain, despite stable analgesic treatment. It is reasonable to use acupuncture for the management of chronic cancer-related pain management. Acupuncture can also be used in conjunction with standard antiemetics to control chemotherapy-related nausea and vomiting.

Alimi D, Rubino C, Pichard-Leandri E, et al. Analgesic effect of auricular acupuncture for cancer pain: a randomized, blinded, controlled trial. *J Clin Oncol.* 2003;21:4120–4126.

Ezzo JM, Richardson MA, Vickers A, et al. Acupuncture-point stimulation for chemotherapy-induced nausea or vomiting. *Cochrane Database Syst Rev.* 2006;(2):CD002285.

C. Complications

C.1. What are the complications of acupuncture treatment?

Acupuncture is safe. Occasionally, although rarely, a patient may have some bruising at an acupuncture site, which is quickly resolved. The principal risk is infection from the use of improperly sterilized needles. This can be avoided by using disposable sterile acupuncture needles and through the practice of proper insertion of the needles. Extremely rare reports have documented pneumothorax caused by improperly inserted acupuncture needles.

A study of the adverse effects of 34,000 acupuncture consultations in the United Kingdom revealed that the most common adverse events were bleeding, needling pain, and aggravation of symptoms. None of these events were serious. Similarly, a review of nine surveys showed that the most common adverse events were needle pain, tiredness, and bleeding. Feelings of faintness and syncope were uncommon. Feelings of relaxation were reported by as many as 86% of patients. The report of pneumothorax was extremely rare, occurring only twice in nearly a quarter of a million treatments.

A study was conducted involving a prospective postal audit of treatments performed by 1,848 professional acupuncturists in the United Kingdom over a 4-week period. They reported 43 minor adverse events, a rate of 1.3 per 1,000 treatments. The events report included severe nausea and fainting, prolonged aggravation of the symptoms, and pain and bruising. The overall frequency of acupuncture-related adverse events is extremely low, and prospective studies have indicated that even

minor adverse events are uncommon. Acupuncture is considered to be a very safe intervention when applied appropriately, and adverse effects of acupuncture are extremely rare.

Ernst E, White A. Prospective studies of the safety of acupuncture: a systemic review. *Am J Med*. 2001;110:481–485.

MacPherson H, Thomas K, Walters S, et al. The York acupuncture safety study: prospective survey of 34,000 treatments by traditional acupuncturists. *Br Med J*. 2001;323:486–487.

Von Riedenauer WB, Baker MK, Brewer RJ, Video-assisted thoracoscopic removal of migratory acupuncture needle causing pneumothorax. *Chest*. 2007;131:899–901.

SECTION XII

Miscellaneous

CHAPTER 52

Myasthenia Gravis

Cephas P. Swamidoss and Cynthia A. Lien

A 25-YEAR-OLD WOMAN

who was gravida 3, para 2 with a 24-week intrauterine fetal demise, presented for dilation and evacuation in the setting of a history of increasing diplopia and dysphagia. She had a known history of myasthenia gravis (MG), diagnosed previously, and underwent a thymectomy for thymoma during the first trimester of her second pregnancy 2 years ago. Since then, she had been in remission and on no medications. Her vital signs were as follows: pulse rate, 60 beats per minute; blood pressure, 150/80 mm Hg; and respiratory rate, 20 breaths per minute. Her arterial oxygen saturation was 98% on room air. She is 155 cm tall and weighs 65 kg.

A. Medical Disease and Differential Diagnosis

1. What is the clinical course of MG?
2. What is the etiology of MG and how is the diagnosis made?
3. What should be included in this patient's differential diagnosis?
4. What is the difference between MG and Lambert-Eaton syndrome?
5. What is the incidence of MG?
6. Describe the clinical classification of MG.
7. How is myasthenia classified in children?
8. What treatment regimens are available for patients with MG?
9. What are the electrical and humoral events that take place during normal neuromuscular transmission? How are these altered in patients with MG?
10. What is the role of surgery in the treatment of MG?
11. What is the effect of pregnancy on the course of MG?
12. What is the effect of MG on pregnancy?

B. Preoperative Evaluation and Preparation

1. How should you assess these patients preoperatively?
2. What preoperative laboratory data are required?
3. Should this patient be premedicated?

C. Intraoperative Management

1. How should this patient be monitored intraoperatively?
2. What anesthetic regimen would you choose for this patient?
3. Can neuromuscular blocking agents be used in patients with MG?

D. Postoperative Management

1. Would you anticipate that this patient will require prolonged postoperative ventilatory support?
2. How should this patient's postoperative pain be treated?
3. This patient was extubated in the operating room without difficulty, and 40 minutes later, she complained of feeling weak and unable to breathe. Why?

A. Medical Disease and Differential Diagnosis

A.1. What is the clinical course of MG?

The hallmark of the symptoms of MG is fluctuating muscle weakness that worsens with exertion and improves after a period of rest. Patients with MG are strongest after resting and therefore feel energized immediately after waking from sleep. Their weakness worsens as the day progresses.

The presentation of MG is usually insidious, occurring over months to years. The initial symptoms are commonly ocular and consist of ptosis and diplopia. Ptosis can be unilateral or bilateral, symmetric or asymmetric, and typically alternates between eyes. The diplopia is usually intermittent. Extraocular muscle involvement can vary from single muscle paresis to total ophthalmoplegia. Muscle fatigue can result in nystagmus. The pupil is usually spared in MG. Ocular symptoms usually progress to more generalized ones in 80% to 85% of patients with MG. The prognosis is better if the symptoms remain confined to those associated with ocular disturbances for more than 2 years.

Involvement of the bulbar muscles produces dysarthria, dysphagia, and difficulty chewing. Weight loss may occur as a result of decreased oral intake and nasal regurgitation, and a nasal twang in the voice can indicate palatal weakness. Involvement of the facial muscles, particularly the elevators of the angles of the mouth (levator labii superioris and levator anguli oris), results in the characteristic myasthenia "snarl."

Although limb muscle weakness occurs in only 15% to 20% of myasthenics, it can manifest as the inability to do simple everyday tasks such as pulling, reaching, or lifting. Proximal muscles are more commonly involved than distal muscles. Rarely, weakness of the neck extensor muscles (rectus capitis posterior major, rectus capitis posterior minor) may occur. Patients affected in this way are unable to keep their heads upright.

Respiratory muscle weakness presents as dyspnea, particularly in the supine position. If the diaphragm is involved, there is a decreased forcefulness of cough and an inability to project the voice.

Many factors may exacerbate the symptoms of MG. These include physical and emotional stress; infection; exposure to bright sunlight; and, particularly in the case of predominantly ocular symptoms, any increase in temperature associated with infection and hyperthyroidism. Medications, including quinidine, procainamide, aminoglycosides, penicillamine, and calcium channel blockers, can also worsen symptoms.

An infection treated with an offending antibiotic may be enough to exacerbate severe respiratory compromise and may necessitate mechanical ventilation.

Drachman DB. Myasthenia gravis. *N Engl J Med*. 1994;330:1797–1810.

Hirsch NP. Neuromuscular junction in health and disease. *BJA*. 2007;99:132–138.

Jani-Acsadi A, Lisak RP. Myasthenia gravis. *Curr Treat Options Neurol*. 2010;12:231–243.

Scherer K, Bedlack RS, Simel DL. Does this patient have myasthenia gravis? *JAMA*. 2005;293:1906–1914.

Schwendimann RN, Burton E, Minagar A. Management of myasthenia gravis. *American J Ther*. 2005;12:262–268.

A.2. What is the etiology of MG and how is the diagnosis made?

MG is an autoimmune disease caused by an antibody to T cell and blockade of nicotinic acetylcholine receptor (AChR) of the motor endplate. Antibodies are detected in 80% of patients with generalized weakness and 50% of patients with ocular disease only. T-cell stimulation is theorized to occur after sensitization within the thymus to a protein similar or identical to the embryonic AChR. In approximately 85% of patients with MG, pathologic alterations of the thymus gland are found: 10% tumors and 75% hyperplasia of lymphoid follicles within the medullas of the thymus. Blockade of AChR results in abnormally decreased membrane motor endplate potential because of a reduction in the number of functional AChRs at the neuromuscular junction. This decreased neurotransmission at the neuromuscular junction causes the clinical symptoms of muscle fatigue in patients with MG.

A diagnosis of MG is usually made by history and clinical examination. It is then confirmed with several diagnostic tests. Clinical tests of stress endurance include monitoring a prolonged upward gaze, holding an outstretched hand in abduction, and determination of vital capacity. These tests provide objective information about fatigability. Other tests that confirm a diagnosis of MG include the following:

- Electrophysiologic tests
- Pharmacologic tests
- Serologic tests

Electrophysiologic testing involves stimulation of a peripheral nerve with a supramaximal stimulus of 2 Hz four times over 2 seconds in a train-of-four pattern. A decrease in twitch response of more than 10%, when the fourth response is compared with the first, is diagnostic of MG. Patients with MG also show less posttetanic facilitation than their healthy counterparts. The sensitivity of this stimulation test is 50% to 70%.

Single-fiber electromyography is a more sensitive electrophysiologic test. It evaluates the time interval between two muscle fiber action potentials in the same motor unit. Because the same nerve innervates both muscle fibers, the time variation between their action potentials, known as "jitter," is a manifestation of neuromuscular junction transmission. In patients with MG, the "jitter" is increased. The sensitivity of this test is higher than 90%, although it is not specific for MG.

Pharmacologic testing involves the administration of the anticholinesterase edrophonium. For this diagnostic test, the patient is fatigued with a task that can be easily assessed, such as slurred speech or vital capacity, and then is given edrophonium. Patients with myasthenia show dramatic improvement within 2 minutes with intravenous administration of 2.5 to 9 mg of edrophonium.

The curare test may also be used to demonstrate that impulse transmission can be markedly reduced at the neuromuscular junction in patients with MG. This test is rarely used because of the associated morbidity and mortality. Serologic testing

involves identification of AChR antibodies. Antibodies to AChR are a serum marker for the diagnosis of MG and are detected in 80% of patients with generalized MG and 50% of patients with only ocular symptoms. Antibodies to striated muscle are also detected in patients with MG, and their presence in high titers usually is associated with thymoma. Although the antibody level does not correlate with disease severity or the patient's prognosis, the antibody tests are still more specific than any other test for MG.

Drachman DB. Myasthenia gravis. *N Engl J Med.* 1994;330:1797–1810.

Fleisher L, ed. *Anesthesia and Uncommon Diseases.* 5th ed. Philadelphia: WB Saunders; 2006:303–325.

Jani-Acsadi A, Lisak RP. Myasthenia gravis. *Curr Treat Options Neurol.* 2010;12:231–243.

Schwendimann RN, Burton E, Minagar A. Management of myasthenia gravis. *Am J Therapeut.* 2005;12:262–268.

A.3. What should be included in this patient's differential diagnosis?

A number of disorders mimic MG and should be included in the initial differential diagnosis. Botulism and Lambert-Eaton syndrome (LES) can cause both weakness and ophthalmoplegia. Botulism affects cranial nerves early. A change in pupillary light response and an increased response on repetitive nerve stimulation can differentiate it from MG.

LES causes a distal muscle weakness that improves after exercise. It is associated with oat cell tumor of the lung in 50% of cases. It is also associated with a defect in the autonomic nervous system, which manifests as dry mouth, orthostatic hypotension, and urinary retention.

Thyrotoxicosis can present with generalized weakness and abnormal thyroid function. Patients with neurasthenia characteristically have weakness, which disappears when individual muscle groups are tested. Progressive external ophthalmoplegia, restricted cardiomyopathies, muscular dystrophies, brain tumors, amyotrophic lateral sclerosis, myasthenic polymyopathy with hypersensitivity to neostigmine, and drugs such as D-penicillamine, aminoglycosides, quinine, procainamide, and calcium channel blockers can also cause myasthenia-like symptoms.

Drachman DB. Myasthenia gravis. *N Engl J Med.* 1994;330:1797–1810.

Eisenkraft JB. Anesthetic considerations in patients with myasthenia gravis. *Cardiothorac Vasc Anesth Update.* 1990;1:1.

Fleisher L, ed. *Anesthesia and Uncommon Diseases.* 5th ed. Philadelphia: WB Saunders; 2006:303–325.

Goetz CJ, Pappert EJ, eds. *Textbook of Clinical Neurology.* Philadelphia: WB Saunders; 1999:1025–1026.

Green DM. Weakness in the ICU. *Neurologist.* 2005;11:338–347.

A.4. What is the difference between MG and Lambert-Eaton syndrome?

Characteristics of MG and LES are presented in Table 52.1.

Book WJ, Abel M, Eisencraft JB, eds. Anesthesia and neuromuscular diseases. *Anesthesiol Clin North Am.* 1996;14:3.

Fleisher L, ed. *Anesthesia and Uncommon Diseases.* 5th ed. Philadelphia: WB Saunders; 2006:303–325.

Table 52.1 Characteristics of Myasthenia Gravis and Lambert-Eaton Syndrome

	MYASTHENIA GRAVIS	LAMBERT-EATON SYNDROME
Gender most commonly affected	Female	Male
Age at onset	20–40 yr	50–70 yr
Presenting signs	Weakness of ocular, bulbar, and facial muscles; fatigue with activity; muscle pains are uncommon; normal tendon reflexes	Weakness and fatigability of the proximal muscles; transient increase in strength on activity; muscle pains common; tendon reflexes reduced or absent
Pathology	Thymus gland most often abnormal, with 15%–20% of patients having thymoma	Small cell carcinoma of the lung usually present
Electromyographic response	Voltage decrement to repeated stimulation, with a good response to anticholinesterases	Voltage increment to repeated stimulation and a poor response to anticholinesterases
Response to muscle relaxants	Increased sensitivity to non-depolarizing neuromuscular blocking agents and a variable response to succinylcholine	Sensitivity to nondepolarizing neuromuscular blocking agents and a normal to increased response to succinylcholine
Presence of antibodies	Antibodies to the acetylcholine receptor present	Antibodies to calcium channel–associated protein synaptogamin are present
Abnormality of autonomic nervous system	Not present	Present
Treatment	Corticosteroids, plasmapheresis, azathioprine, and thymectomy	Corticosteroids, plasmapheresis, azathioprine, and 3,4-diaminopyridine

Healy T, Cohen P, eds. *Wylie and Churchill-Davidson's a Practice of Anesthesia*. 6th ed. London: Edward Arnold; 1995:143.

Hirsch NP. Neuromuscular junction in health and disease. *Br J Anaesth*. 2007;99:132–138.

Titulaer MJ, Soffietti R, Dalmau J, et al. Screening for tumours in paraneoplastic syndromes: report of an EFNS Task Force. *Eur J Neurol*. 2011;18:19–27.

Yanoff M, Duker JS, eds. *Ophthalmology*. London: Mosby; 1999:

A.5. What is the incidence of MG?

MG is relatively rare and has an incidence of approximately 1 in 30,000 people. One and a half times more women than men develop the disease. Men who have this disease have a higher incidence of thymoma. There is a bimodal pattern of incidence, which varies with the sex of the patient. Among women, it occurs within the second and third decade of life—the primary reproductive decades of life. In men, it is seen more commonly in the fifth and sixth decade. Patients younger than 16 years account for less than 10% of cases of myasthenia.

Patients with MG tend to have a higher incidence of autoimmune diseases. These include autoimmune thyroid disease, rheumatoid arthritis, systemic lupus

erythematosus, and diabetes mellitus, suggesting a partial genetic predisposition for myasthenia.

Ferrero S, Pretta S, Nicoletti A, et al. Myasthenia gravis: management issues during pregnancy. *Eur J Obstet Gynecol Reprod Biol.* 2005;121:129–138.

Goetz CJ, Pappert EJ, eds. *Textbook of Clinical Neurology.* Philadelphia: WB Saunders; 1999:1025–1026.

Gurjar M, Jagia M. Successful management of pregnancy-aggravated myasthenic crisis after complete remission of the disease. *Aus N Z J Obstet Gynaecol.* 2005;45:331–332.

Sthoeger Z, Nieman A, Elbirt D, et al. High prevalence of systemic lupus erythematosus in 8 myasthenia gravis patients: a clinical and serological study. *Am J Med Sci.* 2006;331:4–9.

A.6. Describe the clinical classification of MG.

Myasthenia Gravis Foundation of America Clinical Classification

Class I: Any eye muscle weakness, possible ptosis, all other muscle strength is normal
Class II: Mild weakness of other muscles, may have eye muscle weakness of any severity
- IIa: Predominantly limb or axial muscles or both
- IIb: Predominantly oropharyngeal or respiratory muscles or both

Class III: Moderate weakness of other muscles, may have eye muscle weakness of any severity
- IIIa: Predominantly limb or axial muscles or both
- IIIb: Predominantly oropharyngeal or respiratory muscles or both

Class IV: Severe weakness of other muscles, may have eye muscle weakness of any severity
- IVa: Predominantly limb or axial muscles or both
- IVb: Predominantly oropharyngeal or respiratory muscles or both; use of feeding tube without intubation

Class V: Intubation needed to maintain airway

Jaretzki A 3rd, Barohn RJ, Ernstoff RM, et al. Myasthenia gravis: recommendations for clinical research standards. Task force of the medical advisory board of Myasthenia Gravis Foundation of America. *Neurology.* 2000;55:16–23.

Jaretzki A 3rd, Barohn RJ, Ernstoff RM, et al. Myasthenia gravis: recommendations for clinical research standards. Task force of the medical advisory board of Myasthenia Gravis Foundation of America. *Ann Thorac Surg.* 2000;70:327–334.

A.7. How is myasthenia classified in children?

In pediatric patients, MG is classified as transient neonatal, neonatal persistent, or juvenile.

Transient neonatal MG occurs in 21% of infants born to mothers with MG. Most of these infants have circulating AChR antibodies that have been passively transferred from mother to baby. The antibodies are transient. The symptoms with which they present include a feeble cry, poor feeding effort, respiratory difficulty, general or facial weakness, and ptosis. These symptoms last an average 18 days.

Neonatal persistent MG is very rare. Onset is at 2 to 3 months of age. These patients have no detectable antibodies to AChR.

Juvenile myasthenia is very similar to the MG in adults.

Ferrero S, Pretta S, Nicoletti A, et al. Myasthenia gravis: management issues during pregnancy. *Eur J Obstet Gynecol Reprod Biol.* 2005;121:129–138.

Fleisher L, ed. *Anesthesia and Uncommon Diseases.* 5th ed. Philadelphia: WB Saunders; 2006:303–325.

Papazian O. Transient neonatal myasthenia gravis. *J Child Neurol.* 1992;7:135–141.

A.8. What treatment regimens are available for patients with MG?

Multiple forms of treatment for MG are available. They can be broadly classified as follows:

- Pharmacologic
- Surgical
- Plasmapheresis

Pharmacologic treatment with anticholinesterases and immunosuppressants is aimed at manipulation of ACh levels and the immune system.

Anticholinesterases have been used as the initial therapy for symptoms of MG since 1934. By inhibiting the enzymatic metabolism of ACh, these drugs prolong the duration of ACh at the postsynaptic membrane of the neuromuscular junction. Because patient response to these agents is variable, varying from patient to patient and within a patient over the course of a day, patients' education and their involvement in their medical care are required for optimal use of anticholinesterases.

The most common side effects of anticholinesterases are due to the muscarinic effects of ACh and include bradycardia, gastrointestinal cramps, bronchospasm, and an increase in oral and respiratory secretions. The increase in oral secretions can be problematic, particularly for those patients who have bulbar symptoms with already compromised swallowing and in those with respiratory muscle involvement.

Excessive therapy with anticholinergic agents can result in a cholinergic crisis. This will manifest as profound weakness and is due to excess ACh at the neuromuscular junction, which produces a persistent depolarization of the muscle fiber. These symptoms may start a vicious cycle of treating the weakness as myasthenic weakness with anticholinesterases and further exacerbating the cholinergic crisis. In distinguishing clinically between the two, pupillary size may offer some clue to the etiology of the weakness. Hypercarbia in patients with MG causes sympathetic stimulation and dilation of pupils. In a cholinergic crisis, ACh causes constriction of the pupils. It should be noted that patients with primarily ocular symptoms often respond poorly to cholinesterase inhibitors.

Pyridostigmine (Mestinon) is the most commonly used drug for treatment of myasthenia because it causes fewer muscarinic side effects than neostigmine. Its onset of action is 15 to 30 minutes after oral administration, the peak effect is within 1 to 2 hours, and the duration of action is 3 to 4 hours. It is available in three doses (10, 30, and 60 mg), and the typical daily doses range between 30 and 120 mg divided into three to six doses over 24 hours. A long-acting, 180-mg slow-release preparation can be used overnight. A long-acting form of pyridostigmine is also available. Unless the patient has profound morning weakness or nocturnal respiratory distress, it is not commonly used. There is an increased risk for overdosage with the long-acting form of this anticholinesterase.

Edrophonium (Tensilon) 5 to 10 mg intravenously has been used between regularly scheduled doses of anticholinesterases to determine whether the patient is receiving too much or too little medication.

Anticholinesterases do not have an impact on the primary pathology, which is immunologic, and are rarely used alone.

Corticosteroids are used to complement, rather than replace, anticholinesterase therapy. Seventy to eighty percent of patients have complete remission of their disease within weeks to months of treatment with adequate doses of prednisone. Clinical improvement after initiation of corticosteroid therapy is slow and may take weeks. Starting with small doses of corticosteroids can minimize an initial deterioration in a patient's condition. Corticosteroids exert their immunosuppressive effects at many levels of the immune system. They reduce the amount of AChR antibodies and diminish the anti-AChR reactivity of the peripheral blood lymphocytes.

Several different dosing regimens have been suggested. An alternate-day regimen lessens the degree of side effects. The common side effects seen with high-dose corticosteroids are generalized immunosuppression, infection, cataracts, myopathy, osteoporosis, diabetes, and peptic ulcer disease. Most patients require approximately 40 to 60 mg of prednisone per day.

Cytotoxic drugs such as azathioprine and cyclosporine are used in conjunction with corticosteroids and anticholinesterases to reduce the total dose of corticosteroids. Azathioprine acts predominantly on T cells. It is useful in patients in whom corticosteroids are contraindicated. Although it is well tolerated by patients, many months to a year may be required to see its maximal therapeutic effect. Cyclosporine inhibits the production of interleukin-2 by helper T cells. Its efficacy is similar to that of azathioprine, but its maximal therapeutic effect is seen within 1 to 2 months. Its side effects include nephrotoxicity and hypertension.

Adrenocorticotropic hormone (corticotropin) has been used in the treatment of severe MG and is often useful when previous therapy with corticosteroids has failed. This form of treatment, however, is being replaced with plasmapheresis.

Plasmapheresis has been found to effectively remove circulating antibodies and is typically reserved to stabilize patients undergoing myasthenic crisis or preoperatively in patients with severe weakness. After therapy, a patient's condition improves rapidly, but the effects are short lived. When plasmapheresis is used in conjunction with pooled intravenous immunoglobulins in doses of 400 mg/kg/day for 5 days on alternating days, there is a rapid improvement that can last for several weeks.

With an increasing understanding of the immune system, there are some novel potential treatments for MG, such as targeting the specific T and B cells and a nonselective removal of helper T cells, which are responsible for producing the antibodies to AChR. Induction of tolerance to self-antigens by their ingestion has been shown to prevent MG in animal models.

Kumar V, Kaminski HJ. Treatment of myasthenia gravis. *Curr Neurol Neurosci Rep*. 2011; 11:89–96.

Schwendimann RN, Burton E, Minagar A. Management of myasthenia gravis. *Am J Therapeut*. 2005;12:262–268.

Tackenber B, Hemmer B, Oertel WH, et al. Immunosuppresive treatment of ocular myasthenia gravis. *BioDrugs* 2001;15:369–378.

A.9. What are the electrical and humoral events that take place during normal transmission? How are these altered in patients with MG?

Normally, the charge inside a cell is negative relative to the extracellular environment. The potential difference is 70 to 90 mV. During an action potential, the ionic fluxes that occur cause the interior of the cell to become positive by approximately 40 mV. The nerve action potentials cause the release of quanta of ACh from nerve terminals. The ACh crosses the synaptic cleft and attaches to the receptor site on the sarcolemma, causing depolarization. This depolarization is called the *endplate potential*. If the

threshold for excitation is exceeded by the summation of many *endplate potentials*, an action potential invades the muscle cell membrane and spreads along its surface, causing muscle contraction.

In MG, the amount of ACh released from the presynaptic sites is normal or even increased. There are, nevertheless, histologic alterations found at the neuromuscular junctions to which alterations in transmission of impulses can be attributed. These consist of a widening of the synaptic space at the neuromuscular junction and a degeneration of the junctional folds. Most importantly, the concentration of the functional AChRs on the postsynaptic membrane is often reduced by more than 70%. Antibodies to the AChR are responsible for this decrement. These AChR antibodies are directed against various epitopes on the postsynaptic receptor. They decrease the amount of functioning ACh by a number of mechanisms, which include direct blockade, complement-mediated lysis, and increased receptor degradation rate.

Atlee JL, ed. *Complications in Anesthesia*. Philadelphia: WB Saunders; 1998:490–493.

Drachman DB. Myasthenia gravis. *N Engl J Med*. 1994;330:1797–1810.

A.10. What is the role of surgery in the treatment of MG?

Although the efficacy of thymectomy is based on retrospective data, it is a widely accepted therapy for myasthenic patients, particularly those with thymoma and early-onset generalized MG. Thymectomy has been used as a treatment for MG since 1939, when the removal of a cyst from the thymus of a patient with MG, described by Blalock, resulted in remission of the disease. The goal of thymectomy as a treatment for MG is to induce remission, permitting a reduction in the immunosuppressive medication. From 50% to 80% of patients undergoing thymectomy will demonstrate clinical improvement after thymectomy, and 21% to 38% of patients will go into clinical remission (compared with the 13% of medically treated patients).

The exact role of the thymus in the pathogenesis of MG is likely the T-cell–mediated production of AChR antibodies. Thymic epithelial cells and AChRs share similar epitopes. A thymoma is seen in 15% of patients with MG, and thymic hyperplasia is seen in 80% of patients. That clinical improvement frequently seen after thymectomy is further evidence of an association of the thymus in MG. Therefore, thymectomy may be a logical choice for most patients with MG. It is not done in prepubertal children and in those patients with predominantly ocular symptoms. Furthermore, if the symptoms of the disease respond to medical management, patients are not candidates for surgery.

The surgical approach to thymectomy for MG can be either transsternal or transcervical. The transsternal approach allows for better surgical exposure and a more thorough excision. The main advantage of the transcervical approach is that it is minimally invasive. Mortality with this approach is close to 0%, versus 9% with the transsternal approach. Furthermore, the incidence of requiring postoperative ventilation is 10% after transcervical thymectomy, compared with 50% after the transsternal approach. The rates of remission with the two surgical approaches are comparable. Thymectomy may induce perioperative myasthenic crises. Optimizing medical therapy preoperatively may minimize this risk.

Antevil JL, Carroll CG, Roberts PF, et al. Myasthenia gravis: an unexpected cause of respiratory failure and reversible left ventricular dysfunction after cardiac surgery. *J Card Surg*. 2010;25:662–664.

Atlee JL, ed. *Complications in Anesthesia*. Philadelphia: WB Saunders; 1998:490–493.

Fleisher L, ed. *Anesthesia and Uncommon Diseases*. 5th ed. Philadelphia: WB Saunders; 2006:303–325.

Kissel JT, Franklin GM. Treatment of myasthenia gravis. *Neurology*. 2000;55:3–4.

Schwendimann RN, Burton E, Minagar A. Management of myasthenia gravis. *Am J Therapeut*. 2005;12:262–268.

A.11. What is the effect of pregnancy on the course of MG?

The course of MG during pregnancy is unpredictable at best; control at the beginning of the pregnancy does not predict exacerbations or remissions. Worsening symptoms occur in one-third of pregnant women. Although these exacerbations can occur at any time, they are more likely to occur during the first trimester or the first month postpartum. Twenty to forty percent of women experience an improvement in symptoms during the second and third trimesters. Puerperal complications, such as infections, seem to increase the risk of exacerbation of MG symptoms and should be promptly recognized and treated. The mortality risk for mothers with MG is inversely correlated to the duration of the disease, with the highest risk being in the first year and the minimal risk 7 years after the onset of the disease.

Batocchi AP, Majolini L, Evoli A, et al. Course and treatment of myasthenia gravis during pregnancy. *Neurology*. 1999;52:447–452.

Djelmis J, Sostarko M, Mayer D, et al. Myasthenia gravis in pregnancy: report on 69 cases. *Eur J Obstet Gynecol Reprod Biol*. 2002;104:21–25.

Ellison J, Thompson AJ, Walker ID, et al. Thrombocytopenia and leucopenia precipitated by pregnancy in a woman with myasthenia gravis. *BJOG*. 2000;107:1052–1054.

Ferraro S, Pretta S, Noicoletti A, et al. Myasthenia gravis: management issues during pregnancy. *Eur J Obstet Gynecol Reprod Biol*. 2005;121:129–138.

Hoff JM, Dalveit AK, Gilhus NE. Myasthenia gravis: consequences for pregnancy, delivery and the newborn. *Neurology*. 2003;61:1362–1366.

O'Carroll P, Bertorini TE, Jacob G, et al. Transient neonatal myasthenia gravis in a baby born to a mother with new-onset anti-MuSK-mediated myasthenia gravis. *J Clin Neuromusc Dis*. 2009;11:69–71.

Saint-Faust M, Perelman S, Dupont D, et al. Transient neonatal myasthenia gravis revealing a myasthenia gravis and a systemic lupus erythematosus in the mother: case report and a review of the literature. *Am J Perinatol*. 2010;27:107–110.

A.12. What is the effect of MG on pregnancy?

The effect of MG on pregnancy is relatively small. There is no increase in the rate of spontaneous abortion or low birth weight children. Although MG does not increase the rate of premature birth, there is some suggestion of an increased rate of premature rupture of membranes among women with MG. This etiology is unclear, but some think it is related to the course of medications taken by the mother with MG. Case reports of preeclampsia in the setting of MG have been documented, but no study has proven an increased risk resulting from MG. It is recommended that pregnant patients with MG have frequent follow-up with their obstetricians, every 2 weeks in the first and second trimesters and every week in the third trimester. Ultrasound evaluations are necessary during pregnancy to detect signs of fetal akinesia. Fetal monitoring for signs of hypoxia is also very important during myasthenic exacerbations.

Ellison J, Thompson AJ, Walker ID, et al. Thrombocytopenia and leucopenia precipitated by pregnancy in a woman with myasthenia gravis. *BJOG*. 2000;107:1052–1054.

Ferraro S, Pretta S, Noicoletti A, et al. Myasthenia gravis: management issues during pregnancy. *Eur J Obstet Gynecol Reprod Biol.* 2005;121:129–138.

Hoff JM, Dalveit AK, Gilhus NE. Myasthenia gravis: consequences for pregnancy, delivery and the newborn. *Neurology.* 2003;61:1362–1366.

Wen JC, Liu TC, Chen YH, et al. No increased risk of adverse pregnancy outcomes for women with myasthenia gravis: a nationwide population based study. *Eur J Neurol.* 2009;16:889–894.

B. Preoperative Evaluation and Preparation

B.1. How should you assess these patients preoperatively?

The preoperative interview should be used to identify factors that may be predictive of the need for postoperative ventilation. These factors include duration and severity of the disease and the total daily requirement of pyridostigmine or other medications. This information can guide the anesthesiologist in formulating the anesthetic plan, choosing preoperative medications, and appropriately arranging for postoperative care. Patients with MG are usually knowledgeable about their medication; they often are able to adjust their own regimen on the basis of their clinical status.

Whether to alter a patient's anticholinesterase medication preoperatively is still much debated. In patients with mild symptoms, discontinuation of anticholinesterase would seem to be preferable because its continued use can complicate anesthesia by rendering patients more susceptible to vagal arrhythmias. Furthermore, anticholinesterase inhibits plasma cholinesterase and acetylcholinesterase. Because of this, the metabolism of ester local anesthetics, succinylcholine, and mivacurium may be slowed. Certainly, patients who are dependent on their medication should continue it. In this case, the anesthesiologist needs to be aware that postoperative requirements may be markedly reduced. Whether the patient is taking or has taken corticosteroids in the past year should also be determined.

Because other autoimmune diseases occur with increased frequency in patients with myasthenia and can have their own anesthetic implications, evidence of hypothyroidism, pernicious anemia, systemic lupus erythematosus, and rheumatoid arthritis should be sought.

Fleisher L, ed. *Anesthesia and Uncommon Diseases.* 5th ed. Philadelphia: WB Saunders; 2006:303–325.

Miller RD, ed. *Miller's Anesthesia.* 7th ed. Philadelphia: Churchill Livingstone; 2010:1032–1033, 1180–1181.

B.2. What preoperative laboratory data are required?

The need for laboratory studies should be tailored to the patient's history. In addition to routine preoperative laboratory data, patients with MG should have electrolyte abnormalities ruled out, particularly hypokalemia, which can exacerbate weakness. Because many of these patients are on corticosteroids, blood glucose levels should be determined. Cyclosporine trough levels should be obtained to adjust dosing and avoid toxic levels. Blood counts and hepatic and renal function should also be checked.

If the patient will require a general anesthetic for the surgical procedure, a preoperative arterial blood gas analysis and pulmonary function tests would serve as baseline for extubation, particularly if it is anticipated that the patient will be mechanically ventilated postoperatively. By definition, patients with thymomas have an anterior mediastinal

mass that should be evaluated for tracheal compression and deviation. This may affect the ease of endotracheal intubation. Patients with MG can have intrathoracic airway or vascular obstruction on anesthetic induction. Flow–volume loops preoperatively can indicate whether the obstruction is intrathoracic or extrathoracic.

B.3. Should this patient be premedicated?

A preoperative visit should include explanation of the anesthetic procedure and the possibility of postoperative ventilation. Often, these measures serve to allay anxiety and decrease the need for preoperative sedation. Medications that cause respiratory depression should be avoided. Glycopyrrolate can be given to reduce the increased secretions resulting from treatment with anticholinesterases. Stress-dose corticosteroids should be given in the perioperative period for patients who are taking corticosteroids preoperatively.

Fleisher L, ed. *Anesthesia and Uncommon Diseases*. 5th ed. Philadelphia: WB Saunders; 2006:303–325.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:1032–1033, 1180–1181.

C. Intraoperative Management

C.1. How should this patient be monitored intraoperatively?

These patients should be monitored with an electrocardiogram, blood pressure cuff, pulse oximeter, esophageal temperature, and end-tidal capnography. Depending on the nature of the procedure and the severity of the patient's myasthenia, an arterial line may be warranted to monitor arterial blood gases during the processes of weaning from mechanical ventilation and extubation of trachea.

A nerve stimulator should be used to monitor muscle strength even if muscle relaxants are not used intraoperatively. Inhalational anesthetics have been shown to cause depression of the twitch response in the absence of a muscle relaxant in patients with MG. They are extremely sensitive to the neuromuscular junction–depressing properties of volatile anesthetics.

Fleisher L, ed. *Anesthesia and Uncommon Diseases*. 5th ed. Philadelphia: WB Saunders; 2006:303–325.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010;1032–1033, 1180–1181.

C.2. What anesthetic regimen would you choose for this patient?

Multiple options are available for anesthetizing this patient, ranging from a general endotracheal tube anesthetic to a Proseal laryngeal mask airway to regional anesthesia and even monitored anesthesia care. The decision regarding what is right for this patient in this situation depends on weighing the risks for pregnancy-induced aspiration with the anesthetic risks associated with MG, particularly in the postoperative period. The most conservative anesthesia providers would place the risks for aspiration above those of MG and proceed with a general endotracheal anesthetic. Others would weigh the aspiration risks with those of the difficult airway in a pregnant woman or those of postoperative complications resulting from MG and plan for a regional or monitored care anesthetic. There is no correct answer.

Whatever the chosen course, the anesthetic regimen for this patient should be planned to provide the least and briefest interference with ventilatory and neuromuscular function.

In the setting of a general anesthetic, the patient should be preoxygenated before induction of anesthesia with agents such as thiopental, propofol, or etomidate. Opioids should be used cautiously because these patients are very sensitive to their respiratory depressant effects. Ventilation with 100% oxygen should be assisted, and then controlled as necessary. Once an adequate airway is established, a volatile anesthetic can be added to the oxygen. Muscle relaxants are rarely required for laryngoscopy and intubation if the patient is sufficiently anesthetized. Four percent topical lidocaine may be sprayed onto the vocal cords before intubation. Ventilation should be controlled to ensure adequate gas exchange, and anesthesia should be maintained with oxygen, nitrous oxide, and a volatile anesthetic with or without a continuous infusion of a short-acting intravenous anesthetic. Desflurane and an intermediate-acting muscle relaxant have been reported as an effective combination. Dexmedetomidine or propofol may be considered for total intravenous anesthesia–based techniques. Remifentanil, with its short duration of action, may be an appropriate choice of opioid in these patients. As surgery is completed, the anesthesia is tapered to allow for prompt emergence. The patient should not be extubated until awake and responsive, strong, and able to generate a negative inspiratory force of at least -30 cm H_2O. Additionally, the patient should be able to maintain normal oxygenation and normocapnia before extubation of his trachea.

If a regional anesthetic is chosen, either an epidural or a spinal anesthetic, depending on the dermatomal level achieved, preservation of the thoracic muscles may be desirable in preserving the greatest amount of ventilatory function.

Almeida C, Coutinho E, Moreira D, et al. Myasthenia gravis and pregnancy: anaesthetic management—a series of cases. *Eur J Anaesthesiol.* 2010;27:985–990.

Ferrero S, Pretta S, Nicoletti A, et al. Myasthenia gravis: management issues during pregnancy. *Eur J Obstet Gynecol Reprod Biol.* 2005;121:129–138.

Fleisher L, ed. *Anesthesia and Uncommon Diseases.* 5th ed. Philadelphia: WB Saunders; 2006:303–325.

Gurjar M, Jagia M. Successful management of pregnancy-aggravated myasthenic crisis after complete remission of the disease. *Aus N Z J Obstet Gynaecol.* 2005;45:331–332.

Miller RD, ed. *Miller's Anesthesia.* 7th ed. Philadelphia: Churchill Livingstone; 2010:1032–1033, 1180–1181.

C.3. Can neuromuscular blocking agents be used in patients with MG?

The response of the patient with myasthenia to muscle relaxants is altered because of the inherent disease process and because of treatment with anticholinesterase agents. The depolarizing muscle relaxant succinylcholine has been used to facilitate endotracheal intubation. Nevertheless, patients with myasthenia have a variable response to succinylcholine that depends on their medical treatment. In patients not receiving anticholinesterases, the decreased number of functional receptors makes the endplates "resistant" to the effects of succinylcholine. The dose therefore needs to be increased to reliably facilitate intubation. In patients treated with anticholinesterases, plasma cholinesterase activity is decreased. Therefore, more succinylcholine reaches the motor endplate. As succinylcholine metabolism is decreased in these patients, the neuromuscular block can be prolonged from 4 to 87 minutes. Formation of a phase II block has been reported to occur after a single intubating dose of 0.5 mg per kg of succinylcholine. Although the use of succinylcholine is not contraindicated in patients with MG, some clinicians prefer not to use it because of the risk of prolonged neuromuscular block.

In contrast to what is seen after the administration of succinylcholine, the response of the patient with MG to nondepolarizing drugs is extremely predictable. They are exquisitely sensitive to the nondepolarizing drugs and frequently demonstrate a profound weakness after administration of a precurarizing dose of muscle relaxant. This sensitivity is due to the fact that the number of AChRs is decreased by up to 70% in these patients. The number of available receptors is just sufficient to produce endplate potentials that are above the threshold required for neuromuscular transmission and muscle contraction. This reduced receptor concentration reduces the dose of relaxant required for muscle relaxation. Blockade of 70% of receptors, or an effective decrease in the number of receptors by this same amount, will cause a fade in the mechanomyographic response to a train-of-four stimuli in patients without MG.

Despite this increased sensitivity to nondepolarizing muscle relaxants, they can be safely used in patients with MG. Markedly decreased doses should be used. Pancuronium has been reported to cause 95% neuromuscular blockade with only one-fourth of the usual dose used for maintenance of neuromuscular block (0.005 to 0.01 mg per kg). The intermediate-acting muscle relaxants may be more suitable for patients with MG because of their shorter duration of action. Doses ranging from 10% to 50% of those required in patients without myasthenia were used, and prompt extubation was accomplished after either spontaneous recovery or antagonism of the residual neuromuscular block. Because of the metabolism of mivacurium by plasma cholinesterase, it may not be well suited for patients with MG.

Blitt CD, Wright WA, Peat J. Pancuronium and the patient with myasthenia gravis. *Anesthesiology*. 1975;42:624–626.

Buzello W, Noeldge G, Krieg N, et al. Vecuronium for muscle relaxation in patients with myasthenia gravis. *Anesthesiology*. 1986;64:507–509.

Fleisher L, ed. *Anesthesia and Uncommon Diseases*. 5th ed. Philadelphia: WB Saunders; 2006:303–325.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:1032–1033, 1180–1181.

Nilsson E, Meretoja OA. Vecuronium dose response and maintenance requirements in patients with myasthenia gravis. *Anesthesiology*. 1990;73:28–32.

Vacanti CA, Ali HH, Schweiss JF, et al. The response of myasthenia gravis to atracurium. *Anesthesiology*. 1985;62:692–694.

D. Postoperative Management

D.1. Would you anticipate that this patient will require prolonged postoperative ventilatory support?

Predictive criteria for the need for prolonged postoperative ventilatory support have been proposed. Leventhal, Orkin, and Hirsch assigned a scoring system to four factors as follows:

Duration of more than 6 years: 12 points
History of chronic obstructive pulmonary disease: 10 points
Pyridostigmine, more than 750 mg per day: 8 points
Vital capacity less than 2.9 L: 4 points

Patients scoring less than 10 points in their series could be extubated immediately after surgery; those scoring more than 12 points required postoperative ventilatory support. This system of predicting whether a patient will require prolonged intubation and ventilation is not universally applicable. Patients undergoing transsternal

thymectomy require postoperative ventilation more frequently than those undergoing transcervical thymectomy, perhaps because the less invasive procedure has less of an effect on respiratory function.

Similarly, patients with myasthenia undergoing an upper abdominal operation are more likely to require postoperative ventilation than patients undergoing a more peripheral procedure. Obviously, each patient must be considered individually when assessing the need for postoperative ventilatory support.

Eisencraft JB, Papasetas AE, Kahn CH, et al. Predicting the need for postoperative mechanical ventilation in myasthenia gravis. *Anesthesiology.* 1986;65:79–82.

Eisencraft JB, Papasetas AE, Posner JN, et al. Prediction of ventilatory failure following transcervical thymectomy in myasthenia gravis. *Ann N Y Acad Sci.* 1987;505:888.

Fleisher L, ed. *Anesthesia and Uncommon Diseases.* 5th ed. Philadelphia: WB Saunders; 2006: 303–325.

Grant RP, Jenkins LC. Prediction of the need for postoperative mechanical ventilation in myasthenia gravis. A dose response study. *Anesthesiology.* 1988;69:760.

Leventhal SR, Orkin FK, Hirsch RA. Prediction of the need for post operative ventilation in myasthenia gravis. *Anesthesiology.* 1980;53:26–30.

Miller RD, ed. *Miller's Anesthesia.* 7th ed. Philadelphia: Churchill Livingstone; 2010:1032–1033, 1180–1181.

D.2. How should this patient's postoperative pain be treated?

The patient's postoperative analgesic regimen should be designed to avoid any respiratory compromise. Because these patients are exquisitely sensitive to the respiratory depressant effects of parenteral opioids, these should be used sparingly. Epidural administration of opioids is an alternative to parenteral administration. They may provide better pain relief with smaller doses of medication and therefore cause less ventilatory depression.

Fleisher L, ed. *Anesthesia and Uncommon Diseases.* 5th ed. Philadelphia: WB Saunders; 2006:303–325.

D.3. This patient was extubated in the operating room without difficulty, and 40 minutes later, she complained of feeling weak and unable to breathe. Why?

The anesthesiologist needs to determine whether this exacerbation of weakness is due to a cholinergic crisis or a myasthenic crisis. During myasthenic crisis, patients have a decreased response to anticholinesterases. A cholinergic crisis is caused by an overdose of anticholinesterases. Either can be suspected in the immediate postoperative period, when the stress of surgery can cause an exacerbation of myasthenic weakness and when anticholinergic requirements may be altered. In either case, increased muscle weakness may require ventilatory support.

With either myasthenic or cholinergic crisis, increases in muscle weakness, salivation, and sweating occur. It has been recommended that the two crises be differentiated from each other on the basis of the patient's response to an intravenously administered dose of 10 mg of edrophonium. The patient in a myasthenic crisis should show some improvement in muscle strength. The patient in cholinergic crisis will show either no increase in muscle strength or a worsening of respiratory distress.

Fleisher L, ed. *Anesthesia and Uncommon Diseases.* 5th ed. Philadelphia: WB Saunders; 2006:303–325.

CHAPTER 53

Malignant Hyperthermia

HENRY ROSENBERG AND VINOD MALHOTRA

A 7-YEAR-OLD BOY

with kyphoscoliosis was scheduled for ambulatory surgery for repair of strabismus under general anesthesia. Previous anesthetic history included an uneventful sevoflurane and nitrous oxide anesthesia for bilateral myringotomy. The mother was very nervous because a first cousin of the boy had died under anesthesia in Wisconsin the previous year.

A. Medical Disease and Differential Diagnosis

1. What was the problem of concern in this case?
2. What is malignant hyperthermia (MH)?
3. What are the clinical features of a susceptible patient?
4. Does the history of previous uneventful sevoflurane anesthesia reasonably exclude the patient's susceptibility to MH?
5. What are the clinical features of the syndrome?
6. What are the laboratory findings during an acute crisis of MH?
7. What is the incidence of this syndrome?
8. What is the mode of inheritance of the disease? Does MH skip generations?
9. What genetic disorder results in MH susceptibility?
10. What is the pathophysiology of the syndrome?
11. What laboratory tests can further substantiate the susceptibility of the patient to MH?
12. What is neuroleptic malignant syndrome?

B. Preoperative Evaluation and Preparation

1. How would you prepare this patient for anesthesia and surgery?
2. Is dantrolene prophylaxis indicated?
3. What laboratory tests would you obtain before surgery?
4. Is outpatient surgery appropriate for this patient?
5. In anticipation of general anesthesia, what preparations would you make?

C. Intraoperative Management

1. What anesthetic techniques and agents would you employ?
2. Should body (core) temperature be monitored during general anesthesia lasting more than a short time?
3. What anesthetic agents are contraindicated?
4. If the surgeon wants to use local anesthesia for a procedure, what agents will you recommend?
5. What is the significance of masseter muscle spasm occurring after succinylcholine administration?
6. Twenty minutes into the procedure with sevoflurane anesthesia, the patient developed increasing tachycardia with ventricular premature beats and mottled skin. What emergency measures would you take?
7. What modalities would you monitor closely during management of the crisis?
8. What steps should be taken to avoid major morbidity from MH?

D. Postoperative Management

1. What complications may follow this syndrome?
2. What would be your follow-up in this case?
3. What would you advise the patient and the family?
4. What precautions should an MH susceptible patient take out of the OR?

A. Medical Disease and Differential Diagnosis

A.1. What was the problem of concern in this case?

The patient was a 7-year-old boy with kyphoscoliosis and strabismus and a history of an anesthetic-related death in the family in Wisconsin. Therefore, in addition to the respiratory problems associated with kyphoscoliosis, he presented a likelihood of susceptibility to MH syndrome. The supporting factors for strong suspicion were the family history, kyphoscoliosis, and geographic location. There is a high density of MH–susceptible families in the state of Wisconsin.

Li G, Brady JE, Rosenberg H, et al. Excess comorbidities associated with MH in children. *Anesthesiol News*. 2010;36:7.

Rosenberg H, Sambuughin N, Dirksen RA. Malignant Hyperthermia Susceptibility. In: *GeneReviews*. Baskin P, Pagan R, eds. Genetests.org, 2009.

Wedel DJ. Malignant Hyperthermia and Neuromuscular Disease. *Neuromusc Disord*. 1992;2:157–164.

A.2. What is malignant hyperthermia (MH)?

MH, first described by Denborough and Lovell in 1960, is an inherited clinical syndrome characterized by elevated core temperature, tachycardia, tachypnea, hypercarbia, rigidity, acidosis, and hyperkalemia. The underlying abnormality relates to an uncontrolled elevation of intracellular calcium in skeletal muscle cells leading to activation of muscle contractile elements and hypermetabolism. These changes are reversed with the administration of dantrolene, but in the absence of timely treatment, death is likely. In almost every instance, the clinical syndrome occurs in a susceptible patient when a "triggering" anesthetic agent is employed. Not all signs appear in all cases. In rare situations, an MH crisis has appeared in humans in the absence of anesthetic drugs.

Denborough MA, Lovell RRH. Anesthetic deaths in a family [letter]. *Lancet* 1960;2:45.

Muldoon S, Sambuughin N, Bayarsaikhan M, et al. A novel ryanodine receptor (RYR1) variant in two children with fatal spontaneous MH like events. *Anesthesiology* 2008;109:A648.

Rosenberg H, Brandom B, Sambuughin NK. Malignant hyperthermia and other inherited disorders. In: Barash P, Cullen B, Stoelting R, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:598–621.

A.3. What are the clinical features of a susceptible patient?

A family history, if present, particularly in a first-degree relative, is a strong indicator of MH susceptibility. Epidemiologic studies have demonstrated that certain comorbidities such as scoliosis and muscle disorders are more frequent in MH–susceptible individuals. A few myopathic disorders are known to be associated with MH susceptibility. They include central core disease, King-Denborough syndrome, and multiminicore disease (Table 53.1). Nevertheless, most patients susceptible to MH do not have obvious musculoskeletal disorders or a positive family history.

Patients who have Duchenne or Becker muscular dystrophy should not be anesthetized with MH trigger agents because hyperkalemia and rhabdomyolysis may result.

Larach MG, Gronert GA, Allen GC, et al. Clinical presentation, treatment, and complications of malignant hyperthermia in North America from 1987 to 2006. *Anesth Analg*. 2010;110:498–507.

McCarthy TV, Quane KA, Lynch PJ. Ryanodine receptor mutations in malignant hyperthermia and central core disease. *Hum Mutat*. 2000;15:410–417.

Rosenberg H, Davis M, James D, et al. Malignant hyperthermia. *Orphanet J Rare Dis*. 2007;2:21–35.

A.4. Does the history of previous uneventful sevoflurane anesthesia reasonably exclude the patient's susceptibility to MH?

No, it does not. Cases may occur during a second or subsequent anesthetic course.

Bendixen D, Skovgaard LT, Ording H. Analysis of anaesthesia in patients suspected to be susceptible to malignant hyperthermia before diagnostic in vitro contracture test. *Acta Anaesthesiol Scand*. 1997;41:480–484.

Table 53.1 Associated Musculoskeletal Disorders/Signs in Patients Susceptible to Malignant Hyperthermia

Scoliosis
Hypotonia
Exercise-induced rhabdomyolysis
Central core disease
Multiminicore disease
King syndrome

A.5. What are the clinical features of the syndrome?

The clinical features of malignant hypertension are the result of an uncontrolled, exaggerated, hypermetabolic state triggered by the use of potent inhalation anesthetic agents and succinylcholine. In humans, a few cases of malignant hypertension have been thought to occur as a result of environmental factors other than anesthetic agents. Common manifestations include the following:

Specific for malignant hypertension

- Increase in end-tidal carbon dioxide during constant ventilation (the most sensitive and specific sign)
- Generalized rigidity (extremely high specificity)
- Masseter muscle rigidity
- Increased temperature (not uncommonly higher than 40° C)

Nonspecific

- Tachycardia (the earliest and most consistent clinical sign, though not specific)
- Tachypnea
- Arrhythmias
- Skin mottling
- Profuse sweating
- Altered blood pressure

Hyperkalemic cardiac arrest

Sudden hyperkalemic cardiac arrest has been reported after the administration of MH trigger agents in children with undiagnosed myopathy, especially the dystrophinopathies, Duchenne or Becker muscular dystrophy. This response is not a result of pathophysiologic changes typical for MH, but rather muscle membrane destruction leading to hyperkalemia. The pathways leading to the abnormal response is not clear.

The treatment is similar to treatment for hyperkalemia, that is, glucose and insulin, calcium chloride or gluconate, and hyperventilation.

Gurnaney H, Brown A, Litman RS. Malignant hyperthermia and muscular dystrophies. *Anesth Analg*. 2009;109:1043–1048.

Larach MG, Gronert GA, Allen GC, et al. Clinical presentation, treatment, and complications of malignant hyperthermia in North America from 1987 to 2006. *Anesth Analg*. 2010;110:498–507.

Larach MG, Localio AR, Allen GC, et al. A clinical grading scale to predict malignant hyperthermia susceptibility. *Anesthesiology*. 1994;80:771–779.

Larach MG, Rosenberg H, Gronert GA, et al. Hyperkalemic cardiac arrest during anesthetics in infants and children with occult myopathies. *Clin Pediatr*. 1997:9–18.

Nathan A, Ganesh A, Godinez RI, et al. Hyperkalemic cardiac arrest after cardiopulmonary bypass in a child with unsuspected Duchenne muscular dystrophy. *Anesth Analg*. 2005;100:672–674.

A.6. What are the laboratory findings during an acute crisis of MH?

The laboratory values reflect changes of a hypermetabolic state and muscle tissue damage (Table 53.2). Hence, hypercarbia, respiratory and metabolic acidosis, hyperkalemia, elevated creatine kinase, and myoglobinemia are common findings. If the hyperthermia is extreme, coagulopathy is common.

Table 53.2 The Laboratory Findings of Acute Malignant Hyperthermia

METABOLIC AND RESPIRATORY ACIDOSIS
Arterial blood gases
↓↓ pH
↑↑↑ P_{CO_2}
Mild decreases in P_{O_2}
Electrolytes
↑ K
↑ Ca or decreased
↑ Mg
Serum
↑ Lactate
↑ Pyruvate
↑ Creatine kinase
↑ Lactate dehydrogenase
↑ Aldolase
↑ Myoglobin
Increased international normalized ratio, increased fibrin split products increased prothrombin time, increased partial thromboplastin time.

Ali SZ, Taguchi A, Rosenberg H. Malignant hyperthermia. *Best Pract Res Clin Anesthesiol.* 2003;17:519–533.

Larach MG, Gronert GA, Allen GC, et al. Clinical presentation, treatment, and complications of malignant hyperthermia in North America from 1987 to 2006. *Anesth Analg.* 2010;110:498–507.

A.7. What is the incidence of this syndrome?

The incidence of clinical MH is difficult to measure because many clinical syndromes resemble it, and often the anesthetic management is altered when initial signs suggesting MH are detected. The incidence also depends on the prevalence in a population of genetic mutations causal for MH as well as the prevalence of use of MH trigger agents.

One of the earliest epidemiologic studies of MH was conducted in Denmark, where an estimate of the incidence of fulminant MH was noted to be 1 in 260,000 general anesthetics and 1 in 60,000 anesthetics where succinylcholine was used. The incidence was even higher, that is, 1 in 5,000 anesthetics, when such signs as masseter muscle rigidity, unexplained tachycardia, and unexplained fever were included.

In a province of Quebec, Canada, the prevalence of MH was calculated as 0.2 % of the population based on a detailed genealogic study of families with MH susceptibility.

More recently, genetic studies have suggested that the prevalence of mutations that are causal for MH is 1 in 3,000 in France and in Japan.

The incidence of clinical MH appears to be higher in children and in men. Two recent studies of coded hospital discharge data showed that the prevalence of MH is 1 in 100,000 hospital discharges for adults and 4 per 100,000 discharges for children.

Bachand M, Vachon N, Boisvert M, et al. Clinical reassessment of malignant hyperthermia in Abitibi-Temiscamingue. *Can J Anaesth.* 1997;44:696–701.

Brady J, Sun L, Rosenberg H, et al. Prevalence of malignant hyperthermia in New York state, 2001–2005. *Anesth Analg.* 2009;109:1162–1166.

Monnier N, Krivosic-Horber R, Payen JF, et al. Presence of two different genetic traits in malignant hyperthermia families: implication for genetic analysis, diagnosis, and incidence of malignant hyperthermia susceptibility. *Anesthesiology.* 2002;97:1067–1074.

Ording H. Incidence of malignant hyperthermia in Denmark. *Anesth Analg.* 1985;64:700–704.

Rosero EB, Adesanya AO, Timaran CH, et al. Trends and outcomes of malignant hyperthermia in the United States, 2000 to 2005. *Anesthesiology.* 2009;110:89–94.

A.8. What is the mode of inheritance of the disease? Does MH skip generations?

MH is inherited in humans in an autosomal dominant fashion with reduced penetrance and variable expressivity. It is heterogenetic with up to seven gene loci implicated, but only two are confirmed.

More than 70% of MH cases are linked to the ryanodine receptor gene located on chromosome 19. Less than 2% are related to mutations in the dihydropyridine receptor (*DHPR*) gene. Over 200 mutations have been found in that gene, with up to 30 documented to be causal for the syndrome.

Because MH is inherited in an autosomal dominant manner, the susceptibility to it does not "skip" generations. Nevertheless, because of the low penetrance, not all of those with MH mutations display the syndrome on exposure to trigger agents.

In MH–susceptible pigs, the inheritance is autosomal recessive with only one DNA change noted to account for all cases.

Litman RS, Rosenberg H. Malignant hyperthermia: update on susceptibility testing. *JAMA.* 2005;239:2918–2924.

McCarthy TV, Healey JM, Heffron JJ, et al. Localization of the malignant hyperthermia susceptibility locus to human chromosome 19q12–13.2. *Nature.* 1990;343:562–564.

Sambuughin N, Holley H, Muldoon S, et al. Screening of the entire ryanodine receptor type 1 coding region for sequence variants associated with malignant hyperthermia susceptibility in the North American population. *Anesthesiology.* 2005;102:515–521.

Stewart SL, Hogan K, Rosenberg H, et al. Identification of the Arg1086His mutation in the alpha subunit of the voltage-dependent calcium channel (CACNA1S) in a North American family with malignant hyperthermia. *Clin Genet.* 2001;59:178–184.

A.9. What genetic disorder results in MH susceptibility?

In almost all cases, the MH susceptible patient has a defective calcium channel located in the membrane of the sarcoplasmic reticulum of skeletal muscle. This channel is termed the *ryanodine receptor* because it binds the plant alkaloid ryanodine.

The channel is closely associated with other proteins and structures, such as the dihydropyridine calcium channel that mediates transfer of voltage change to the RYR-1 receptor. Other proteins associated with the ryanodine receptor include triadin and FKB-12 binding protein. Mutations in the *RYR-1* gene are associated with MH susceptibility in more than 65% of patients and their families. Nevertheless, only about 30% of patients with MH harbor a mutation *proven* to lead to increased intracellular calcium on exposure to caffeine or MH trigger anesthetics, the critical criteria to confirm the pathophysiology of MH. Over 200 additional mutations have yet to be characterized regarding the effects on calcium movements. One reason for the slow progress in deciphering the

significance of these many mutations is that, unlike many other conditions, there are many private mutations that predispose to MH. No single mutation accounts for more than about 10% of MH cases. The *DHPR* gene, also involved in intracellular calcium control, has been associated with susceptibility in 1% to 2% of MH–susceptible families.

There are probably other genes that may lead to MH susceptibility but are much less common than those associated with the *RYR-1* and the *DHPR* genes.

Of interest is the observation that mutations associated with central core disease and multiminicore disease, two myopathies that also predispose to MH, are located on the *RYR-1* gene as well. In central core disease, the sarcoplasmic reticulum is depleted of calcium to a significant extent because of the increased permeability of the ryanodine receptor. With a depletion of calcium, muscle contraction is weakened when the muscle is activated.

Recently, genetically engineered mice were developed that include one or more of the mutations causal for MH in the mouse genome. The mice display signs typical of MH during exposure to trigger agents and also on exposure to raised environmental temperature.

Chelu MG, Goonasekera SA, Durham WJ, et al. Heat- and anesthesia-induced malignant hyperthermia in an RyR1 knock-in mouse. *FASEB J.* 2006;20:329–330.

Monnier N, Krivosic-Horber R, Payen JF, et al. Presence of two different genetic traits in malignant hyperthermia families: implication for genetic analysis, diagnosis, and incidence of malignant hyperthermia susceptibility. *Anesthesiology.* 2002;97:1067–1074.

Sambuughin N, Holley H, Muldoon S, et al. Screening of the entire ryanodine receptor type 1 coding region for sequence variants associated with malignant hyperthermia susceptibility in the North American population. *Anesthesiology.* 2005;102:515–521.

A.10. What is the pathophysiology of the syndrome?

The MH syndrome results from an abnormal and uncontrolled elevation of intracellular calcium levels in skeletal muscle. The pathophysiology is as follows: The process of calcium release from the sarcoplasmic reticulum normally begins with depolarization of the sarcolemma that is transmitted via the T tubules to the *DHPR*, which in turn activates the calcium channel termed the ryanodine receptor to release calcium.

The elevated calcium removes the inhibition of actin and myosin interaction that leads to mechanical force generation. The calcium release occurs via a channel within the sarcoplasmic reticulum called the ryanodine receptor. Reuptake of calcium returns the intracellular cytoplasmic concentration of calcium to normal and muscle relaxation takes place. Reuptake is mediated via a calcium adenosine triphosphate (ATP)ase pump mechanism.

A variety of intermediate proteins also regulate the intrasarcoplasmic reticulum concentration of calcium, such as calsequestrin, a calcium-binding protein. Genetically engineered mice that do not express calsequestrin have been shown to develop clinical signs of MH on exposure to trigger anesthetics. It is thought that in the absence of the calcium buffer, intracellular calcium levels increase significantly, but only on exposure to MH triggers.

The control of calcium release is highly regulated because when muscle contraction takes place, a variety of energy-consuming steps are required resulting in ATP breakdown and heat production.

During an MH episode, the ryanodine receptor calcium channel is locked in an open position, leading to an uncontrolled release of calcium with elevation of intracytoplasmic calcium levels and continuous muscle activation as well as ATP breakdown. The sarcoplasmic reticulum calcium pump is unable to resequester the calcium. ATP breakdown during this process aggravates heat production further. Dantrolene reverses these changes.

Energy-consuming processes take place through glycolysis as well as oxidative phosphorylation. Eventually, ATP levels are insufficient to maintain sarcolemmal integrity and potassium leaks from the cell resulting in hyperkalemia. Myoglobinemia occurs for the same reason as does an increase of a number of enzymes, including creatine kinase.

Protasi F, Paolini C, Dainese M. Calsequestrin-1: a new candidate gene for malignant hyperthermia and exertional/environmental heat stroke. *J Physiol*. 2009;587(pt 13): 3095–3100.

Rosenberg H, Brandom BW, Sambuughin NK, Fletcher JE. Malignant hyperthermia and other pharmacogenetic disorders. In: Barash P, Cullen B, Stoelting R, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:598–613.

A.11. What laboratory tests can further substantiate the susceptibility of the patient to MH?

The most accurate diagnostic test for MH is the exposure of biopsied skeletal muscle to halothane, caffeine, and, more recently, ryanodine or chlorocresol. In this test, approximately 1 g of muscle is harvested from the thigh under regional or, in the case of a child, general anesthesia. Strips or fascicles of muscle weighing 100 to 200 mg are suspended in a water bath at 37° C and exposure is made to halothane, caffeine, ryanodine, or chlorocresol in specific graded concentrations. The isometric contracture, not contraction, response to muscle is measured via strain gauge following specific guidelines. The threshold and height of the contracture is measured, and a diagnosis of MH is made based on the contracture threshold and strength exceeding specific values.

The test is highly sensitive, close to 100%, but as many as 20% of positive results are false-positives. Nevertheless, the value of the test resides in ruling out MH susceptibility with certainty.

Because the test is invasive and costly and requires strict adherence to specific requirements, there are only about six testing centers in North America. There are over 20 in Europe. Two slightly different versions of the test exist, the North American and the European versions. The main difference is in the concentration of drugs used during exposure of the muscle and the threshold for determining a positive response.

The patient and history must be carefully evaluated by the biopsy center director before recommending the test in order to enhance accuracy.

Molecular genetic testing for malignant hyperthermia susceptibility

The era of DNA testing for MH susceptibility began in 1990 when a mutation in the *RYR-1* gene was shown to be causal for MH in pigs. In humans, several genes have been associated with MH, though the *RYR-1* gene is probably responsible for most cases. At present, 30 mutations in the *RYR-1* gene have been found in humans that are causal for MH–based on strict criteria related to in vitro calcium release or clinical MH in several generations and families. Unfortunately, no mutation accounts for more than a small percent of all patients with MH susceptibility. The chief advantage of genetic testing is that all that is required is a blood sample, and the specimen may be shipped to the laboratory. The main limitation of genetic testing is the sensitivity of approximately 30%. Undoubtedly, the sensitivity will improve as more mutations are identified and tested for their ability to alter the structure and function of the ryanodine receptor.

Patients should consider genetic testing if:

1. They have had a positive contracture test.
2. A family member has had a positive contracture test.
3. They have suffered a very likely MH episode but have not had a contracture test.
4. A family member has been found to have a causal mutation.

In those patients who are tested and a causal mutation identified, those with the mutation are MH susceptible (high specificity), but those without the mutation *cannot* be considered MH negative because they may harbor another mutation.

At present, there are two clinical testing laboratories for diagnosing MH susceptibility: PreventionGenetics (www.preventiongenetics.com) and the DNA diagnostic laboratory at the University of Pittsburgh (http://path.upmc.edu/divisions/mdx/diagnostics.html).

The decision to undergo genetic testing is complex because the test, although requiring only a blood sample, costs approximately $900 for the search for the most common mutations. Once a mutation is found, the cost for screening family members is $200 each. This compares to an approximate cost of $6,000 for the contracture test. The pros and cons of testing should be discussed with either a MH expert or a genetic counselor.

Allen GC, Larach MG, Kunselman AR. The sensitivity and specificity of the caffeine-halothane contracture test: a report from the North American MH Registry. *Anesthesiology*. 1998;88:579–588.

Girard T, Treves S, Voronkov E, et al. Molecular genetic testing for malignant hyperthermia susceptibility. *Anesthesiology*. 2004;100;1076–1080.

Litman RS, Rosenberg H. Malignant hyperthermia: update on susceptibility testing. *JAMA*. 2005;239:2918–2924.

Rosenberg, H, Antognini JF, Muldoon S. Testing for malignant hyperthermia. *Anesthesiology*. 2002;96:232–237.

A.12. What is neuroleptic malignant syndrome?

The neuroleptic malignant syndrome is also a hypermetabolic syndrome characterized by hyperthermia, rigidity, rhabdomyolysis, acidosis, and tachycardia, features that mimic MH. However, neuroleptic MH is precipitated by a variety of neuroleptic drugs, including haloperidol, the atypical antipsychotics, phenothiazines, and other centrally acting drugs.

This syndrome differs from neuroleptic MH in that central dopamine depletion is responsible for the clinical picture. The mainstays of treatment are benzodiazepines and a dopamine agonist such as bromocriptine. Patients also respond symptomatically to dantrolene therapy. A recent report identified *RYR-1* mutations in a small percentage of patients manifesting neuroleptic MH. Perhaps many more also have these mutations.

A variety of drug-induced hyperthermic syndromes resemble MH such as the serotonin syndrome. The most common situation for the serotonin syndrome is the administration of meperidine in a patient on monoamine oxide inhibitor drugs.

Ecstasy and other methylenedioxymethamphetamine agonists also produce hyperthermia. Again, the signs may resemble MH, but the pathophysiology is very different.

Anesthesiologists may encounter neuroleptic MH in patients who are sedated with haloperidol in the intensive care unit and on infrequent occasions when patients are given dopamine agonist agents such as metoclopramide and promethazine.

Rosebush PI, Garside S, Mazurek MF. Recognizing neuroleptic malignant syndrome. *CMAJ*. 2004;170:1645.

Strawn JR, Keck PE Jr, Caroff SN. Neuroleptic malignant syndrome. *Am J Psych*. 2007;164:870–876.

B. Preoperative Evaluation and Preparation

B.1. How would you prepare this patient for anesthesia and surgery?

Preoperative preparation should include a detailed medical history, assessment of the patient's physical status, evaluation of laboratory findings including creatine kinase, and specific investigations to determine the susceptibility of the patient to MH. Three possible scenarios are as follows:

- The halothane caffeine contracture test result is normal. The patient should be considered not susceptible to MH, and the anesthetic should be nonrestrictive.
- The halothane caffeine contracture test is abnormal, implying MH susceptibility. Or, a mutation associated with MH is identified. In this case, trigger-free anesthetic agents should be employed and all preparations should be made to quickly treat the syndrome if it develops.
- The halothane caffeine contracture test is not available. This is very frequently the case because this test is done in only a few centers in the country. In such situations, the patient should be treated as MH syndrome and all appropriate steps should be followed.

Islander G, Ranklev-Twetman E. Evaluation of anaesthesia in malignant hyperthermia negative patients. *Acta Anaesthesiol Scand.* 1995;39:819–821.

Rosenberg H, Brandom BW, Sambuughin NK, et al. Malignant hyperthermia and other pharmacogenetic disorders. In: Barash P, Cullen B, Stoelting R, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:598–613.

B.2. Is dantrolene prophylaxis indicated?

If a nontriggering anesthetic is administered with appropriate monitoring to an MH–susceptible patient, dantrolene prophylaxis is not necessary.

With the judicious use of trigger-free anesthetics, MH is extremely unlikely. A very rare case or two have been reported of MH without trigger agents; nevertheless, because many syndromes may mimic it, it is not at all clear whether any of the cases were really MH.

Dantrolene can cause side effects, such as nausea, vomiting, pain at the injection site, and depression of the twitch response. In patients with pre-existing muscle weakness, dantrolene may cause respiratory insufficiency in the postoperative period.

Brandom BW, Larach GM, Chen Min-Shue A. Complications associated with the administration of Dantrolene 1987 to 2006: A Report from the North American Malignant Hyperthermia Registry of the Malignant Hyperthermia Association of the United States. *Anesth Analg.* 2011;112:1115–1123.

Lichtman AD, Oribabor C. Malignant hyperthermia following systematic warming after hypothermic cardiopulmonary bypass. *Anesth Analg.* 2006;102:372–375

B.3. What laboratory tests would you obtain before surgery?

Chest radiograph and electrocardiogram should be ordered if dictated by his scoliosis or other associated medical illness. Otherwise, there is no routine laboratory testing indicated for strabismus surgery in this child. Serum creatine kinase level is of value as a baseline test and should be obtained.

B.4. Is outpatient surgery appropriate for this patient?

With the use of trigger-free anesthetics and appropriate monitoring, surgery normally performed in an outpatient setting is acceptable. Postoperative admission to the hospital

solely on the basis of MH susceptibility is not warranted. When MH occurs, it is usually in the immediate postoperative period and usually not beyond 2 hours postoperatively. Therefore, it is prudent to keep the patient longer than usual in the postanesthesia care unit in a monitored setting and a little longer in the ambulatory discharge area.

All ambulatory surgery and office-based surgery settings should have a plan for managing MH and transferring the patient to a hospital.

Pollock N, Langton E, McDonnell N, et al. Malignant hyperthermia and day stay surgery. *Anaesth Intens Care*. 2006;34:40–45.

Yentis SM, Levine MF, Hartley EJ. Should all children with suspected or confirmed malignant hyperthermia susceptibility be admitted after surgery? A 10-year review. *Anesth Analg*. 1992;75:345–350.

B.5. In anticipation of general anesthesia, what preparations would you make?

A satisfactory preparation for administering anesthesia to this patient should include measures to prevent and treat an acute crisis of MH. The following should be available:

Equipment

- Drain, remove, or disable vaporizers.
- Fresh circuit, reservoir bag, and soda lime. Flush machine and ventilator by flowing 10 L oxygen per minute for 10 minutes.
  - For newer anesthesia work stations, the washout period may be prolonged up to 60 minutes. The manufacturers' guidelines for machine preparation should be followed.
  - Activated charcoal filter placed on inspiratory and expiratory limb of the machine
- Routine American Society of Anesthesiologists monitors including:
  - Pulse oximeter
  - Capnometer
  - Core temperature monitor
  - electrocardiogram and blood pressure monitors

Items to have available:

Cooling aids

- Hypothermia blanket
- Crushed ice
- Cold saline for irrigation and intravenous infusion
- Nasogastric tube and Foley catheter for cavity cooling

Drugs

- Sodium bicarbonate, mannitol, furosemide, dantrolene (intravenous), sterile water, antiarrhythmics, insulin, 50% dextrose, and calcium chloride
- *Avoid* calcium channel blockers because of interaction with dantrolene, possibly resulting in cardiac arrest

Beebe JJ, Sessler DI. Preparation of anesthesia machines for patients susceptible to malignant hyperthermia. *Anesthesiology*. 1988;69:395–400.

Birgenheier N, Stoker R, Westenskow D, Orr J, *Anesth Analg*. 2011;112:1363–1370.

Gunter JH, Gall J, Than-Win S. Preparation of the Dräger Fabius anesthesia machine for the malignant–hyperthermia susceptible patient. *Anesth Analg*. 2008;107:1936–1945.

San Juan AC Jr, Wong KC, Port JD. Hyperkalemia after dantrolene and verapamil-dantrolene administration in dogs. *Anesth Analg*. 1988;67:759–762.

C. Intraoperative Management

C.1. What anesthetic techniques and agents would you employ?

Potent inhalation agents and succinylcholine (excluding nitrous oxide) are to be avoided. If possible, local or regional anesthesia is preferred. Anesthesia may be induced with a barbiturate, benzodiazepine, or hypnotic agent and the patient ventilated with 100% oxygen. Fentanyl or other opioid may be added to ensure adequate depth of anesthesia. Topical anesthesia of the larynx and vocal cords may be achieved with a local anesthetic spray. The trachea is intubated with or without the use of a short-acting or intermediate-acting nondepolarizing muscle relaxant. Anesthetic maintenance is achieved using oxygen and nitrous oxide, an opioid, and a nondepolarizing relaxant as required. Total intravenous anesthesia is a good choice for anesthesia as well. Vital signs are monitored with very close attention to capnography.

C2. Should body (core) temperature be monitored during general anesthesia lasting more than a short time?

Definitely. Although temperature elevation is often not the first sign of MH, it is one of the common early signs of the syndrome. Therefore, core temperature, esophageal, axillary, rectal, urinary bladder, nasopharyngeal temperature should be monitored for all procedures lasting more than 30 minutes. In addition, temperature monitoring is also important in detecting hypothermia.

Larach MG, Gronert GA, Brandom BW, Lehman ED. Clinical Presentation, treatment and complications of malignant hyperthermia in North America from 1987–2006. *Anesth Analg*. 2011;112:1115–1123.

C.3. What anesthetic agents are contraindicated?

In general, the anesthetic agents to be avoided include potent inhalation agents and depolarizing muscle relaxants. Of the agents commonly employed today, the following have been implicated in triggering MH:

- Inhalation agents: halothane, enflurane, isoflurane, desflurane, and sevoflurane
- Muscle relaxants: succinylcholine

Fu ES, Scharf JE, Mangar D, et al. Malignant hyperthermia involving the administration of desflurane. *Can J Anaesth*. 1996;43:687–690.

Otsuka H, Komura Y, Mayumi T, et al. Malignant hyperthermia during sevoflurane anesthesia in a child with central core disease. *Anesthesiology*. 1991;75:699–701.

Rosenberg H, Brandom BW, Sambuughin NK, et al. Malignant hyperthermia and other pharmacogenetic disorders. In: Barash P, Cullen B, Stoelting R, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:598–613.

C.4. If the surgeon wants to use local anesthesia for a procedure, what agents will you recommend?

Both ester and amide local anesthetics are now considered safe for use in patients with MH syndrome.

D'Ambrosia J, Adragna MG. Guidelines for the use of local anesthetics in the dental treatment of patients who are susceptible to malignant hyperthermia. *Spec Care Dentist*. 1988;8:61–63.

Maccani RM, Wedel DJ, Melton A, et al. Femoral and lateral femoral cutaneous nerve block for muscle biopsies in children. *Paediatr Anaesth.* 1995;5:223–227.

C.5. What is the significance of masseter muscle spasm occurring after succinylcholine administration?

Rigidity of the jaw muscles after administration of succinylcholine is referred to as *masseter muscle rigidity* (MMR) or trismus. MMR presages clinical MH in up to 30% of cases. Even in the absence of clinical MH, myoglobinuria following succinylcholine-induced MMR is common postoperatively. MMR probably occurs in individuals of all ages, though MMR is more common in children, particularly following gas anesthesia induction.

MMR has been reported in 1% of children after halothane or succinylcholine induction and in adults after succinylcholine administration. Should MMR occur, elective surgery should be postponed, the patient observed in an intensive care unit setting for 24 hours seeking myoglobinuria specifically. The patient should be followed until creatine kinase levels normalize.

In the case of emergency surgery, the anesthetic should be converted to a "non-trigger" technique and the patient observed for early signs of MH. Dantrolene and other treatment procedures for MH should be made ready.

The patient and/or family should be advised to be evaluated for MH susceptibility.

The incidence of MMR and MH episodes in children have recently decreased as a result of recommendations that the use of succinylcholine in children be reserved for emergency situations.

Other causes of succinylcholine-induced MMR include any form of myotonia or periodic paralysis.

Gronert GA, Rosenberg H. Management of patients in whom trismus occurs following succinylcholine. *Anesthesiology.* 1988;68:653–655.

O'Flynn RP, Schutak JG, Rosenberg H. Masseter muscle rigidity and malignant hyperthermia susceptibility in pediatric patients: an update on management and diagnosis. *Anesthesiology.* 1994;80:1228–1233.

Parness J, Bandschapp O, Girard T. The myotonias and susceptibility to malignant hyperthermia. *Anesth Analg.* 2009;109;1054–1064.

Rosenberg H. Trismus is not trivial. *Anesthesiology.* 1987;67:453–455.

C.6. Twenty minutes into the procedure with sevoflurane anesthesia, the patient developed increasing tachycardia with ventricular premature beats and mottled skin. What emergency measures would you take?

Although tachycardia may arise from other, more common causes, such as a light plane of anesthesia or hypovolemia, its association with dysrhythmia in this patient who has MH syndrome raises the suspicion that a MH crisis may be starting. End-expiratory carbon dioxide should be monitored, and if it is rising despite increasing minute ventilation, the diagnosis of MH should be strongly considered. Time is of the essence and this constitutes a critical emergency, so the following steps should be taken:

- Stop all anesthetics and surgery (if possible).
- Hyperventilate the patient with 100% oxygen.
  - Obtain help and assistance through the MH hotline of the Malignant Hyperthermia Association of the United States (MHAUS; 1-800-MH–HYPER).
- Administer specific drug therapy: Start dantrolene sodium early while muscle perfusion is still present. An initial intravenous dose of 2.5 mg per kg should be

followed by repeated doses of 1 to 2 mg per kg to a total of 10 mg per kg depending on the patient's response. More dantrolene may be administered if clinically indicated.

- Initiate aggressive cooling immediately for rapidly increasing temperatures and for those higher than 40° C. Methods for cooling include surface cooling with the patient on a cooling blanket and packed in ice; gastric, rectal, or peritoneal lavage with iced saline; and iced intravenous fluids (saline). Cooling should be stopped when the patient's temperature falls to lower than 38° C to prevent inadvertent hypothermia.
- Treat acidosis with sodium bicarbonate (2 mEq per kg initial dose and titrate as necessary).
- Treat hyperkalemia with hyperventilation, sodium bicarbonate, insulin, and 50% dextrose.
- Treat arrhythmias with standard antiarrhythmics, and avoid calcium channel blockers if dantrolene has been given.
- An arterial line and Foley catheter should be inserted in all cases of fulminant MH. Central venous catheterization should be considered for unstable patients or where aggressive therapy is needed.
- Maintain urine output with mannitol or furosemide.
- Follow creatine kinase levels every 12 hours.
- Check electrolytes and coagulation parameters.
- Register the patient and the event with the North American Malignant Hyperthermia Registry.

Forms may be obtained through MHAUS. The website for the North American Malignant Hyperthermia Registry is www.mhreg.org.

Ali SZ, Taguchi A, Rosenberg H. Malignant hyperthermia. *Best Pract Res Clin Anesthesiol.* 2003;17:519–533.

C.7. What modalities would you monitor closely during management of the crisis?

The modalities that should be monitored closely include the following:

- End-tidal carbon dioxide
- Arterial blood gases/electrolytes/coagulation
- Core temperature
  - Creatine kinase levels
  - Myoglobin levels: urine and serum
  - Urine output

C.8. What steps should be taken to avoid major morbidity from MH?

All sites where general anesthesia is administered should have 36 vials of dantrolene available within about 10 minutes.

All patients undergoing general anesthesia for more than 30 minutes should have core temperature monitored.

All operating rooms (OR) should have an MH drill each year. This drill should involve all OR personnel, going through the steps of alerting the team, obtaining dantrolene, mixing dantrolene, simulating blood draw, cooling the patient, and discussing the episode with family members.

In addition, nonhospital sites should ensure that a hospital is designated to receive a patient who is experiencing an MH episode. The facility should have a plan regarding who will accompany the patient and what drugs and monitors will accompany the

transport personnel. The local hospital personnel must ensure dantrolene is in stock, as well as be familiar with treating the syndrome.

D. Postoperative Management

D.1. What complications may follow this syndrome?

Disseminated intravascular coagulation syndrome is a major complication of MH, especially when the patient's temperature exceeds 41° C. Other complications include renal failure, hyperkalemia, and compartment syndrome. As a result of massive muscle breakdown, the patient may be weak for days and also complain of muscle cramps and pain.

Rosenberg H, Brandom BW, Sambuughin NK, et al. Malignant hyperthermia and other pharmacogenetic disorders. In: Barash P, Cullen B, Stoelting R, eds. *Clinical Anesthesia.* 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:598–613.

D.2. What would be your follow-up in this case?

The vigorous therapy started in the OR should be continued in the immediate postoperative period into the postanesthesia care unit or the intensive care unit. Dantrolene administration should be continued for at least 36 hours after an episode is controlled at a dose of 1 mg per kg every 4 to 6 hours titrated to signs of MH. Serum creatine kinase should be followed until normalized.

Other laboratory values that should be followed until normalized include:

- Arterial blood gases
- Electrolytes
- Coagulation profile

Body temperature should be monitored along with other vital signs. Recrudescence of MH occurs in approximately 25% of treated cases; therefore, the patient should be watched in an intensive care unit setting for at least 36 hours following an episode.

Rosenberg H, Brandom BW, Sambuughin NK, et al. Malignant hyperthermia and other pharmacogenetic disorders. In: Barash P, Cullen B, Stoelting R, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:598–613.

D.3. What would you advise the patient and the family?

The patient and his family should be warned of the dangerous nature of this syndrome and should be advised to carry an identification band at all times. The pedigree of the family should be prepared, and the members should be investigated for susceptibility to this syndrome and issued medical identification bracelets or pendants accordingly.

The MHAUS has been active since 1981 and offers current information and advice on patient management as well as identification bracelets and a variety of materials for healthcare professionals. The following is some useful contact information:

Emergency hotline: 1-800-MH-HYPER
Address: MHAUS, 39 East State Street, P.O. Box 1609, Sherburne, NY 13815
Phone: 1-800-98-MHAUS
Internet: www.mhaus.org

In addition, the patient and his family should consult with one of the MH diagnostic centers to discuss further evaluation. A complete listing is available through MHAUS.

The patient should be registered with the North American Malignant Hyperthermia Registry.
Forms may be obtained through MHAUS.
The website for the North American MH Registry is www.mhreg.org
The phone number is (888) 274-7899
The Registry is located at the Children's Hospital of the University of Pittsburgh.
The director is Dr. Barbara Brandom.

D4. What precautions should an MH susceptible patient take out of the OR?

In general, MH–susceptible patients should be cognizant of their response to heat and exercise. As for any patient, excess exposure to heat and humidity, especially with exercise, should be limited or avoided. Although it is true that a few cases of what appears to be MH have been reported without anesthesia, these are very rare. At present, there is no way to predict which patients may have an adverse response to environmental conditions.

Muldoon S, Sambuughin N, Bayarsaikhan M, et al. A novel ryanodine receptor (RYR1) variant in two children with fatal spontaneous MH like events. *Anesthesiology A*. 2008:648.

Tobin JR, Jason DR, Challa VR, et al. Malignant hyperthermia and apparent heat stroke. *JAMA*. 2001;286:168–169.

CHAPTER 54

Postoperative Residual Neuromuscular Weakness and Prolonged Apnea

David Kopman and Aaron F. Kopman

A HEALTHY 35-YEAR-OLD, 65-kg female was scheduled for an elective abdominal hysterectomy. Anesthesia was induced with propofol 2.0 mg/kg, fentanyl 2.0 μg/kg, and rocuronium 1.2 mg/kg. Anesthesia, which lasted 90 minutes, was maintained with desflurane 5.0% end-tidal and supplemented with fentanyl as needed. At the termination of surgery, residual neuromuscular block was not antagonized as the tidal volume was deemed to be adequate, and the train-of-four count (TOFC) using facial nerve stimulation was four with no detectable fade. Upon arrival in the postanesthesia care unit (PACU), the patient was tachypneic, had uncoordinated and floppy arm movements, and appeared to be agitated and in distress. Arterial oxygen saturation on room air was 89%.

A. Medical Diseases and Differential Diagnosis

1. What is the differential diagnosis for postoperative apnea?
2. How is residual neuromuscular block diagnosed?
3. Do all voluntary muscles respond similarly to nondepolarizing relaxants?
4. If this was an emergency surgery, anesthesia was induced with a rapid sequence technique including succinylcholine. The patient remained apneic not only throughout the procedure but also in the PACU. What was the possible diagnosis? How would you confirm it? How would you manage the patient?
5. What are acetylcholinesterase and serum cholinesterase?
6. What is the incidence of atypical cholinesterase activity?
7. What is the significance of the dibucaine number?
8. What are some factors that can lower pseudocholinesterase levels?
9. What are the side effects of succinylcholine?

B. Intraoperative Management

1. How is the choice among muscle relaxants made?
2. How much do individuals vary in their sensitivity to nondepolarizing relaxants?
3. What are the characteristics of nondepolarizing block?
4. What is a train-of-four (TOF) stimulus?
5. Why is the TOF ratio of clinical importance?
6. How do we define adequate recovery of neuromuscular function?
7. Are there useful and/or trustworthy clinical tests of neuromuscular recovery?
8. How accurate are subjective estimates of the TOF ratio?
9. What is double burst stimulation (DBS)?
10. What is a posttetanic count?
11. What function does the conventional peripheral nerve stimulator (PNS) serve?
12. How can the TOF ratio be measured quantitatively?
13. What are the limitations of anticholinesterase antagonists?
14. Is there anything wrong with administering neostigmine when the TOF count (TOFC) is less than 3?
15. Is reversal of residual block always necessary?
16. Is there any way to rapidly antagonize profound nondepolarizing block?

C. Postoperative Management

1. What is the incidence of residual neuromuscular block in the PACU?
2. Does undetected postoperative residual neuromuscular block have clinical consequences?

A. Medical Diseases and Differential Diagnosis

A.1. What is the differential diagnosis for postoperative apnea?

The differential diagnosis for postoperative apnea includes the following:

- Residual anesthetic agent
- Residual narcotic
- Residual muscle relaxant
- Hypocarbia
- Occurrence of some medical complication during anesthesia, such as stroke or embolism

Miller RD, ed. *Miller's Anesthesia.* 7th ed. Philadelphia: Elsevier Churchill Livingstone; 2010:2710–2711.

A.2. How is residual neuromuscular block diagnosed?

This patient showed clear signs of residual neuromuscular weakness upon arrival in the PACU. TOF stimulation at the ulnar nerve showed a TOFC of only 2 at the adductor pollicis (thumb). A provisional diagnosis of residual nondepolarizing block was made and the patient received neostigmine 0.05 mg/kg plus an appropriate dose of glycopyrrolate, 0.01 mg/kg. Seven minutes later, the TOFC was 4 with no evidence of fade on palpation of the thumb, and all signs of residual block had abated.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier Churchill Livingstone; 2010:2710–2711.

A.3. Do all voluntary muscles respond similarly to nondepolarizing relaxants?

Although facial nerve stimulation is widely used by clinicians to judge the adequacy of block and recovery, this practice can be very misleading. At a time when the TOFC at the orbicularis oculi or corrugator supercilii muscles shows good recovery from nondepolarizing block, the response at the hand may be almost nonexistent. Thus, facial nerve stimulation may give the clinician a false sense of security about the adequacy of neuromuscular recovery at the end of a case.

Similarly, in the intubated patient breathing spontaneously, a normal tidal volume and maintenance of an acceptable P_{CO_2} do not necessarily indicate adequate neuromuscular recovery. The diaphragm is the first muscle to recover from nondepolarizing block and requires significantly higher plasma levels of relaxants to maintain paralysis. The muscles that protect the upper airway are far more sensitive to nondepolarizing relaxants.

Thus, a patient who may be able to maintain adequate respiratory exchange while intubated may experience complete airway obstruction when extubated.

Caffrey RR, Warren ML, Becker KE. Neuromuscular blockade monitoring comparing the orbicularis oculi and adductor pollicis muscles. *Anesthesiology*. 1986;65:95–97.

Cantineau JP, Porte F, d'Honneur G, et al. Neuromuscular effects of rocuronium on the diaphragm and adductor pollicis in anesthetized patients. *Anesthesiology*. 1994;81:585–590.

Donati F, Bevan DR. Not all muscles are the same. *Br J Anaesth*. 1992;68:235–236.

Eikermann M, Blobner M, Groeben H, et al. Postoperative upper airway obstruction after recovery of the train of four ratio of the adductor pollicis muscle from neuromuscular blockade. *Anesth Analg*. 2006;102:937–942.

Stiffel P, Hameroff SR, Blitt C, et al. Variability in assessment of neuromuscular blockade. *Anesthesiology*. 1980:52:436–437.

A.4. If this was an emergency surgery, anesthesia was induced with a rapid sequence technique including succinylcholine. The patient remained apneic not only throughout the procedure but also in the PACU. What was the possible diagnosis? How would you confirm it? How would you manage the patient?

The easiest possibility to exclude is residual neuromuscular block. In the above patient, stimulation of the ulnar nerve with a PNS resulted in no response of the muscles of the hand. Hence, the diagnosis of a prolonged response to succinylcholine was established. Extreme prolongation in succinylcholine's duration of effect is usually a manifestation of an atypical genotype. Following a 1.0 mg/kg dose of succinylcholine in patients homozygous for the most common atypical butyrylcholinesterase genotypes, apnea generally lasts upwards of an hour and it may take as much as 3 hours for adequate respiratory efforts to return. However, the duration of apnea is highly dependent on the butyrylcholinesterase variant in question and may be shorter or longer than the figures just cited.

Traditionally, identification of the human butyrylcholinesterase (BChE) variant has been performed by biochemical analysis. These tests, which have been used for decades, consist of the measurement of plasma cholinesterase activity with different substrates and of testing the degree of inhibition of this activity with a well-known inhibitor, such as dibucaine, fluoride, or R02-0683. These tests have identified multiple genes, which can reside at the same allelic site such as the atypical, silent, fluoride-resistant, J, K,

H, and Newfoundland variants. However, biochemical testing often leads to equivocal results. More recently, molecular biologic techniques have been applied to identifying a patient's exact genotype.

Once the diagnosis of an atypical response to succinylcholine is ascertained, treatment is entirely supportive and symptomatic. Since the duration of residual block is hard to predict, the patient should remain intubated, artificially ventilated, and sedated. Only after a strong, sustained response to indirect tetanic stimulation at the wrist can be demonstrated should sedation be terminated and an attempt made to wean the patient off controlled ventilation. Patients recovering from prolonged succinylcholine-induced block usually exhibit a "dual" or "phase II" block during recovery (fade on repetitive stimulation). While neostigmine or edrophonium can under certain circumstances antagonize this block, this approach is risky when dealing with prolonged succinylcholine apnea. If significant plasma levels of succinylcholine are still present, the administration of an acetylcholinesterase may be counterproductive.

The patient should obviously be informed that he or she had a prolonged episode of muscular weakness, and that the presumptive cause was an atypical reaction to succinylcholine. The patient should be urged to have this diagnosis confirmed and he or she should be directed to an appropriate laboratory. If an atypical genotype is confirmed, he or she should encourage his or her family members to be tested as well. Finally, the patient should be assured that this diagnosis has no adverse health consequences, but that in the future when surgery is planned, his or her anesthesiologist needs to be informed of this diagnosis.

Bevan DR, Donati F. Suxamethonium apnoea: attempted reversal with anticholinesterases. *Can Anaesth Soc J*. 1983;30:536–539.

Cerf C, Mesguish M, Gabriel I, et al. Screening patients with prolonged neuromuscular blockade after succinylcholine and mivacurium. *Anesth Analg*. 2002;94:461–466.

Donati F, Bevan DR. Antagonism of phase II succinylcholine block by neostigmine. *Anesth Analg*. 1985;64:773–776.

Jensen FS, Viby-Mogensen J. Plasma cholinesterase and abnormal reaction to succinylcholine: twenty years' experience with the Danish Cholinesterase Research Unit. *Acta Anaesthiol Scand*. 1995;39:150–156.

La Du BN. Butyrylcholinesterase variants and the new methods of molecular biology. *Acta Anaesthiol Scand*. 1995;39:139–141.

Levano S, Ginz H, Siegemund M, et al. Genotyping the butyrylcholinesterase in patients with prolonged neuromuscular block after succinylcholine. *Anesthesiology*. 2005;102:531–535.

Pantuck EJ. Plasma cholinesterase: gene and variations. *Anesth Analg*. 1993;77:380–386.

"The only satisfactory method of determining the degree of neuromuscular block is to stimulate a motor nerve with an electric current and observe the contraction of the muscles innervated by that nerve." Churchil-Davidson HC. The d-tubocurarine dilemma. *Anesthesiology*. 1965;26:132–133.

Viby-Mogensen J. Correlation of succinylcholine duration of action with plasma cholinesterase activity in subjects with the genotypically normal enzyme. *Anesthesiology*. 1980;53:517–520.

Viby-Mogensen J. Succinylcholine neuromuscular blockade in subjects homozygous for atypical plasma cholinesterase. *Anesthesiology*. 1981;55:429–434.

A.5. What are acetylcholinesterase and serum cholinesterase?

Acetylcholinesterase is a relatively specific enzyme that hydrolyzes acetylcholine (ACh) faster than it does other choline esters. It is found in red blood cells, the central nervous system, and the neuromuscular junction. It is responsible for hydrolyzing and inactivating the ACh produced during normal neuromuscular transmission. It does not hydrolyze succinylcholine and is inhibited by the drug.

Serum cholinesterase, also called *cholinesterase, pseudocholinesterase, butyrylcholinesterase(BChE),* and *nonspecific cholinesterase,* hydrolyzes many choline esters, including succinylcholine. It is found in many human tissues, but not in the red blood cell. It is synthesized in the liver. Its physiologic function is unknown, but it may hydrolyze choline esters, such as propionylcholine and butyrylcholine, which may be formed by bacterial action in the gut and by the enzyme systems responsible for the formation of ACh.

Massoulie J, Bon S. Molecular forms of cholinesterase and acetylcholinesterase in vertebrates. *Annu Rev Neurosci*. 1982;5:57.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier Churchill Livingstone; 2010:347–348, 863–864.

Pantuck EJ. Plasma cholinesterase: gene and variations. *Anesth Analg*. 1993;77:380–386.

Taylor P, Schumacher M, MacPhee-Quingley K, et al. The structure of acetylcholinesterase: relationship to its function and cellular disposition. *Trends Neurosci*. 1987;10:93.

A.6. What is the incidence of atypical cholinesterase activity?

The incidence of atypical cholinesterase activity varies with the population studied, but it is approximately 1 of 2,800 in the general population of the United States, with a 1:1 male/female ratio.

Kalow W, Genest K. A method for detection of atypical forms of human serum cholinesterase: determination of dibucaine numbers. *Can J Biochem*. 1957;35:339.

Maddineni VR, Mirakhur RK. Prolonged neuromuscular block following mivacurium. *Anesthesiology*. 1993;78:1181–1184.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier Churchill Livingstone; 2010:863–864.

A.7. What is the significance of the dibucaine number?

The dibucaine number is used to identify the heterozygote. Dibucaine in 10^{-5} mol per L concentration produces the maximum difference in inhibition between the usual and the atypical forms of serum cholinesterase. The term *dibucaine number* has been applied to the percentage of inhibition of serum cholinesterase. The usual homozygote has a dibucaine number of approximately 80, the atypical homozygote has a value less than 30, and the heterozygote has a value between 45 and 69. The relation between the dibucaine number and the duration of succinylcholine neuromuscular blockade is shown in Table 54.1.

A.8. What are some factors that can lower pseudocholinesterase levels?

Reduced pseudocholinesterase activity may be associated with:

- Abnormal genotype
- Normal physiologic variation (e.g., pregnancy). However, until BChE activity is reduced to <30% of normal, only modest increases in the duration of succinylcholine are to be expected.
- Liver disease
- Malnutrition
- End-stage renal disease
- Burns
- Plasmapharesis
- Noncompetitive cholinesterase inhibitors (e.g., pesticides, certain nerve gases)
- Competitive cholinesterase inhibitors (e.g., neostigmine)

Table 54.1 Relation between Dibucaine Number and Duration of Succinylcholine Neuromuscular Blockade

TYPE OF PSEUDOCHOLINESTERASE	GENOTYPE	FREQUENCY	DIBUCAINE NUMBER[a]	RESPONSE TO SUCCINYLCHOLINE OR MIVACURIUM
Homozygous typical	EuEu	Normal	70–80	Normal
Heterozygous	EuEa	1/480	50–60	Slightly prolonged
Homozygous atypical	EaEa	1/3,200	20–30	Markedly prolonged

[a]The dibucaine number indicates the percentage of enzyme inhibited.

These include liver disease, advanced age, malnutrition, pregnancy, burns, oral contraceptives, monoamine oxidase inhibitors, echothiophate, cytotoxic drugs, neoplastic disease, anticholinesterase drugs, tetrahydroaminacrine, hexafluorenium, and metoclopramide.

Davis L, Britten JJ, Morgan M. Cholinesterase. Its significance in anaesthetic practice. *Anaesthesia*. 1997;52:244–260.

Kalow W, Genest K. A method of detection of atypical forms of human serum cholinesterase: determination of dibucaine numbers. *Can J Biochem*. 1957;35:339–353.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier Churchill Livingstone; 2010:863–864.

A.9. What are the side effects of succinylcholine?

The most common untoward side effect seen after succinylcholine administration is muscle pain occurring in the first 24 to 48 hours postoperatively. Women and patients undergoing ambulatory surgery appear most susceptible to this phenomenon. The reported incidence of succinylcholine-induced myalgia is quite variable but probably occurs in 25% to 50% of patients. Discomfort is typically characterized as being similar to the muscle soreness that occurs after heavy or unusual exercise. It has been postulated that the etiology of the phenomenon is related to muscle damage caused by asynchronous contractions during the initial muscle depolarization that precedes paralysis. Defasciculating doses of nondepolarizing relaxants (10% of the ED95) given 2 to 5 minutes prior to succinylcholine have been shown to reduce the incidence of myalgia by as much as 50%. Pretreatment with nonsteroidal anti-inflammatory drugs have also been shown to reduce the incidence of muscle pain following succinylcholine administration.

Succinylcholine may also be associated with various cardiac dysrhythmias including bradycardia, tachycardia, and junctional and ventricular dysrhythmias. Stimulation of nicotinic receptors at sympathetic and parasympathetic ganglion and muscarinic receptors at the sinus node are believed to be involved in this phenomenon. Infants and children may be more likely to manifest clinically significant bradycardia following succinylcholine administration secondary to their relatively high degree of resting vagal tone as compared to adults. Pretreatment with atropine is effective in preventing succinylcholine-induced bradycardia and is recommended when succinylcholine is to be used in this patient population. Sinus bradycardia in adults is more commonly seen when a second dose of succinylcholine is given approximately 5 minutes after the first. Pretreatment with atropine can prevent this as well. Junctional rhythms following succinylcholine administration are also relatively common. The postulated mechanism

of action is muscarinic stimulation of the sinus node that results in diminished sinus activity and the subsequent emergence of the atrioventricular node as the dominant pacemaker. Various mechanisms have been postulated to explain ventricular dysrhythmias that sometimes occur after succinylcholine administration including potassium release from skeletal muscle, succinylcholine-mediated sensitivity to catecholamines, and profound sinus and atrioventricular node slowing.

The most serious complication associated with succinylcholine administration is severe and potentially lethal levels of hyperkalemia in at-risk individuals. When succinylcholine is administered to an otherwise healthy patient during the induction of anesthesia, plasma potassium levels typically increase by <0.5 mEq/L as potassium ions move from the intracellular to extracellular space. The increase is transient and is typically tolerated well by most patients. In at-risk patients, however, the efflux of potassium from the intracellular space can be in excess of 3.5 mEq/L, enough to induce malignant dysrhythmias and cardiac arrest. The list of susceptible patients includes those with congenital muscular dystrophies, upper or lower motor neuron defects, prolonged chemical denervation (e.g., muscle relaxants, magnesium, clostridial toxins), direct muscle trauma or inflammation, extensive burns, and disuse atrophy. In the event that succinylcholine is inadvertently given to an at-risk patient and an exaggerated hyperkalemic response is suspected, prompt treatment with calcium chloride (1 to 2 g), hyperventilation, sodium bicarbonate (1 mEq/kg), regular insulin, and dextrose should be initiated to prevent severe dysrhythmias and cardiac arrest.

Succinylcholine also causes increases in intraocular, intragastric, and intracranial pressures (ICP). The increase in intraocular pressure caused by succinylcholine begins rapidly after drug administration. Peak pressures may rise as much as 5 to 15 mm Hg before returning to baseline levels about 6 minutes after drug dosing. The etiology of this phenomenon is unclear, but detachment of the intraocular muscles from the globe fails to prevent the pressure rise, which is suggestive of an intraocular mechanism. It has been suggested that succinylcholine use should be avoided in the setting of open-eye injuries, although there is scant evidence that its administration has led to extrusion of intraocular contents or blindness.

The increase in intragastric pressure caused by succinylcholine is likely related to fasciculations of the abdominal skeletal musculature. A defasciculating dose of a nondepolarizing muscle relaxant given prior to succinylcholine administration can prevent any increase in intragastric pressure.

Succinylcholine can also cause a transient increase in ICP. The increase in ICP after succinylcholine administration correlates with muscle fasciculations, increased electroencephalogram activity, and elevated cerebral blood flow. Prior administration of a nondepolarizing muscle relaxant can attenuate or even prevent this pressure increase. The use of succinylcholine in the setting of intracranial hypertension is probably best limited to emergency situations where the benefits of rapid airway control outweigh the risks of a transient increase in ICP.

Lastly, it should be remembered that succinylcholine is a potent trigger of malignant hyperthermia. Its use should be restricted to settings where prompt recognition and treatment of malignant hyperthermia are possible.

Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:505–506.

Cottrell JE, Young WL, eds. *Cottrell and Young's Neuroanesthesia*. 5th ed. Philadelphia: Mosby Elsevier; 2010:87.

Martyn JA, Richtsfeld M. Succinylcholine-induced hyperkalemia in acquired pathologic states: etiologic factors and molecular mechanisms. *Anesthesiology*. 2006;104:158–69.

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Pace NL. Prevention of succinylcholine myalgias: a meta-analysis. *Anesth Analg*. 1990;70:477–83.

Wong SF, Chung F. Succinylcholine-associated postoperative myalgia. *Anaesthesia.* 2000;55:144–152.

Yentis SM. Suxamethonium and hyperkalemia. *Anaesth Inten Care.* 1990;18:92–101.

B. Intraoperative Management

B.1. How is the choice among muscle relaxants made?

A muscle relaxant can be chosen based on onset characteristics, duration of action, and method of metabolism (Table 54.2). Muscle relaxants can be characterized as short, intermediate, and long duration. Metabolism may or may not be dependent on liver and kidney function.

B.2. How much do individuals vary in their sensitivity to nondepolarizing relaxants?

In any group of healthy patients, there exists a wide variability in the sensitivity to the effects of neuromuscular blocking agents (NMBA). The potency of these drugs is expressed as the agent's ED_{50} or ED_{95} (the dose that will produce 50% or 95% depression of a single twitch [T1] in an average individual). The coefficient of variation (the standard deviation as a percentage of the mean value) for the ED_{95} of most agents approximates 20% to 25%. Thus, if the ED_{95} for drug X is 1.0 mg/kg, in 5% of normal individuals, the ED_{95} may be <0.60 mg/kg. Because of the shape of the dose-response curve of nondepolarizing relaxants, this modest difference in drug requirement may have large consequences with regard to the depth of block. In these individuals, a plasma level that produces only 50% block of T1 in the average subject may produce >90% instead.

Similarly, the duration of effect of administered relaxants is quite variable. For example: Following a 1.2 mg/kg dose, the clinical duration of rocuronium (time to 25% T1 recovery) in a sample size of only 12 averaged 67 minutes; however, the range in responses went from 39 to 118 minutes.

Following a dose 2 × the ED_{95} of a blocker of intermediate duration (e.g., vecuronium), 30% of individuals will still need pharmacologic antagonism 2 hours later.

In the aged or in patients with renal or hepatic disease, this variability is even more pronounced. This is especially true of aminosteroid blockers such as vecuronium or rocuronium when compared with atracurium or cisatracurium.

Arain SR, Kern S, Ficke DJ, et al. Variability of duration of action of neuromuscular-blocking drugs in elderly patients. *Acta Anaesth Scand.* 2005;49:312–315.

Debaene B, Plaud B, Dilly MP, et al. Residual paralysis in the PACU after a single intubating dose of nondepolarizing muscle relaxant with an intermediate duration of action. *Anesthesiology.* 2003;98:1042–1048.

Kopman AF, Kahn N, Neuman GG. Precurarization and priming: a theoretical analysis of safety and timing. *Anesth Analg.* 2001;93:1253–1256.

Puhringer FK, Heier T, Dodgson M, et al. Double-blind comparison of the variability in spontaneous recovery of cisatracurium- and vecuronium-induced neuromuscular block in adult and elderly patients. *Acta Anaesthesiol Scand.* 2002;46:364–371.

Wright PMC, Caldwell JE, Miller RD. Onset and duration of rocuronium and succinylcholine at the adductor pollicis and laryngeal adductor muscles in anesthetized humans. *Anesthesiology.* 1994;81:1110–1115.

B.3. What are the characteristics of nondepolarizing block?

The distinguishing feature of nondepolarizing block is fade on repetitive stimulation. For example, consider a situation in which the amplitude of twitch height (T1) is

Table 54.2 Characteristics of Commonly Used Muscle Relaxants

DRUG	ED_{95} UNDER N_2O/O_2 (mg/kg)	DOSE FOR INTUBATION (mg/kg)	INTUBATION TIME (sec)	CLINICAL DURATION (min)	METABOLISM (%)	ELIMINATION	
						KIDNEY (%)	LIVER (%)
Ultrashort acting							
Succinylcholine	0.5	1.0	60	5–10	Plasma cholinesterase (98–99)	<2	0
Short acting							
Mivacurium	0.08	0.2–0.25	120	12–15	Plasma cholinesterase (95–99)	<5	0
Intermediate acting							
Vecuronium	0.05	0.1–0.2	120	45–60	Liver (30–40)	40–50	50–60
Rocuronium	0.3	0.6–1.0	90	45–55	None	<10	>70
Cisatracurium	0.05	0.15–0.2	120	45–60	Hofmann elimination (77)	16	–
Long acting							
α-Tubocurarine	0.5	0.5–0.6	150	100–120	None	80	20
Pancuronium	0.07	0.08–0.12	150	100–120	Liver (10–20)	85	15
Pipecuronium	0.05	0.08–0.10	180	100–120	10	>90	<10
Doxacurium	0.025	0.05–0.08	240	120–150	None	>90	<10

From Miller RD, ed. *Miller's Anesthesia.* 7th ed. Philadelphia: Elsevier Churchill Livingstone; 2010:872–880.

reduced by 50% with a nondepolarizing blocker when stimuli are delivered at 0.10 Hz (1 every 10 seconds). If the rate of stimulation is increased to 1 Hz, the height of T1 may fall to <20% of control, and at 2 Hz to about 10% of control. This fade is most easily appreciated subjectively when tetanic stimuli (rates ≥30 Hz) are delivered.

Lee C, Katz RL. Fade of neurally evoked compound electromyogram during neuromuscular block by d-tubocurarine. *Anesth Analg.* 1977;56:271–275.

B.4. What is a train-of-four (TOF) stimulus?

A "train-of-four" consists of four stimuli delivered at half-second intervals (2 Hz). The TOF ratio is the height of the fourth indirectly elicited response divided by the amplitude of the first response. This ratio in unparalyzed individuals normally approximates a value of 1.0 when measured by mechanomyography (MMG), electromyography (EMG), or kinemyography but may exceed a value of 1.10 when measured by acceleromyography (AMG) (see below). As the depth of block increases, this ratio becomes smaller and eventually the fourth, then the third, and so on responses "drop out." If only two responses to a TOF stimulus are present, we speak of a TOFC of 2.

Ali HH, Utting JE, Gray TC. Stimulus frequency in the detection of neuromuscular block in man. *Br J Anaesth.* 1970;42:967–978.

B.5. Why is the TOF ratio of clinical importance?

The TOF fade is a far more sensitive index of residual block than singletwitch depression. In addition, the TOF ratio is useful because each TOF sequence serves as its own control. It is not necessary to know the amplitude of the evoked response prior to relaxant administration, or to worry about baseline drift over time.

Traditionally, the TOF ratio is measured at the hand by noting the response of thumb adduction. While clinicians are much more interested in the neuromuscular function of the diaphragm, masseter, and laryngeal adductors, correlations with adductor pollicis muscle function have over time served as useful clinical surrogates for the muscles we really care about.

Ali HH, Utting JE, Gray TC. Quantitative assessment of residual antidepolarizing block. I. *Br J Anaesth.* 1971;43:473–477.

Kopman AF. Surrogate endpoints and neuromuscular recovery. *Anesthesiology.* 1997;87:1029–1031.

B.6. How do we define adequate recovery of neuromuscular function?

Once the TOF ratio at the adductor pollicis has recovered to a value of 0.70, tests of mechanical respiratory reserve such as vital capacity and peak expiratory flow rate have usually recovered to within 90% of control. At a TOF value of 0.70, recovery of single twitch to control height and a sustained response to tetanic stimulation at 50 Hz for 5 seconds is usually present.

The studies done in the 1970s thus suggested that a TOF ratio of 0.70 was synonymous with adequate neuromuscular recovery and this was the accepted standard for the next two decades. However, by the late 1990s, this assumption was questioned. Work in awake volunteers demonstrated that at a TOF ratio of 0.70, grip strength was decreased by more than 40%. At a TOF ratio of 0.70, the vast majority of subjects had

difficulty apposing their incisor teeth and could not sip water from a straw because they could not make a tight seal around the straw with their lips. All individuals had double vision at TOF ratio <0.90. It was clear that these health volunteers were not "street ready" until their TOF ratios reached or exceeded a value of 0.90. In addition, other volunteer studies revealed even more alarming data. At a TOF ratio of 0.70, there is a decreased response in the ventilatory response to hypoxia (via a mechanism at the carotid body), and the swallowing mechanism becomes disorganized. Partial paralysis (a TOF of 0.70) causes pharyngeal dysfunction and increased risk for aspiration at mechanical adductor pollicis TOF ratios <0.90. Pharyngeal function is not normalized until an adductor pollicis TOF ratio of >0.90 is reached. Thus, the current standard for adequate neuromuscular recovery is a TOF ratio of 0.90 or better.

Ali HH, Kitz RJ. Evaluation of recovery from non-depolarizing neuromuscular blockade using a digital neuromuscular analyser: preliminary report. *Anesth Analg.* 1973; 52:740–744.

Ali HH, Wilson RS, Savarese JJ, et al. The effect of d-tubocurarine on indirectly elicited train-of-four muscle response and respiratory measurements in humans. *Br J Anaesth.* 1975;47:570–574.

Brand JB, Cullen DJ, Wilson NE, et al. Spontaneous recovery from nondepolarizing neuromuscular blockade: correlation between clinical and evoked responses. *Anesth Analg.* 1977;56:55–58.

Eriksson LI, Sato M, Severinghaus JW. Effect of a vecuronium-induced partial neuromuscular block on hypoxic ventilatory response. *Anesthesiology.* 1993;78:693–699.

Eriksson LI, Sundman E, Olsson R, et al. Functional assessment of the pharynx at rest and during swallowing in partially paralyzed humans. Simultaneous videomanometry and mechanomyography of awake human volunteers. *Anesthesiology.* 1997;87:1035–1043.

Kopman AF, Yee PS, Neuman GG. Correlation of the train-of-four fade ratio with clinical signs and symptoms of residual curarization in awake volunteers. *Anesthesiology.* 1997;86:765–771.

B.7. Are there useful and/or trustworthy clinical tests of neuromuscular recovery?

The first commercially available PNS did not appear until the mid-1960s, and units capable of delivering TOF stimuli did not arrive for another decade. Even today, devices that can quantify or measure the TOF ratio in real time are not widely distributed. Thus, clinicians have been reluctant to abandon clinical tests of neuromuscular recovery first suggested half a century ago: tidal volume, negative inspiratory force, grip strength, the 5-second head lift, the ability to protrude the tongue and so on. Unfortunately, most of these tests share one fundamental weakness. They require an awake and cooperative patient. Ideally, we would like to know the state of neuromuscular recovery prior to awakening the patient and certainly prior to tracheal extubation.

The most widely cited test (the 5-second head lift) is clearly not a sensitive test of residual block. At a TOF ratio of 0.50, the majority of patients may still pass this test.

Other widely mentioned tests are no better and may actually be very misleading. Traditional "bedside" tests of residual muscle weakness lack sensitivity and must be considered unreliable.

Beemer GH, Rozental P. Postoperative neuromuscular function. *Anaesth Intens Care.* 1986;14:41–45.

Dupuis JY, Martin R, Tétrault JP. Clinical, electrical and mechanical correlations during recovery from neuromuscular blockade with vecuronium. *Canad J Anaesth.* 1990;37:192–196.

El Mikatti N, Wilson A, Pollard BJ, et al. Pulmonary function and head lift during spontaneous recovery from pipecuronium neuromuscular block. *Br J Anaesth.* 1995;74:16–19.

B.8. How accurate are subjective estimates of the TOF ratio?

Unfortunately, visual or tactile estimations of the TOF ratio are notoriously inaccurate. Once the TOF ratio exceeds a value of 0.40 to 0.50, a majority of experienced anesthetists are unable to detect the presence of any fade at all. Thus, failure to detect fade made indicate a true value anywhere from 0.50 to 1.0. Accurate assessment of the TOF ratio requires an objective or quantitative monitor (see later in this chapter).

Viby-Mogensen J, Jensen NH, Engbaek J, et al. Tactile and visual evaluation of the response to train-of-four nerve stimulation. *Anesthesiology.* 1985;63:440–443.

B.9. What is double burst stimulation (DBS)?

Because of the limitations in subjective interpretation of TOF fade, other patterns of stimulation have been investigated. A somewhat more sensitive test is the response to DBS. This sequence consists of a very brief tetanic pulse (3 stimuli at 50 Hz), and a 0.75-second pause followed by another brief tetanus. This is felt by the observer as two strong twitches. Most observers lose the ability to detect DBS fade at a TOF ratio of about 0.60.

Engæk J, Østergaard D, Viby-Mogensen J. Double burst stimulation (DBS): a new pattern of nerve stimulation to identify residual neuromuscular block. *Br J Anaesth.* 1989;62:274–278.

B.10. What is a posttetanic count?

As the level of neuromuscular block is progressively deepened, the TOFC eventually falls to zero. No response to TOF stimulation can be elicited. Because posttetanic potentiation is a prominent feature of nondepolarizing block, it is still possible, however, to get additional information about the depth of block. The following sequence is employed: a 5-sec 50-Hz tetanus, a 3-second pause, then 20 stimuli at 1 Hz. The number of responses elicited is referred to as the posttetanic count. Generally, when the count approximates a value of 10, the first response to TOF stimulation appears.

Viby-Mogensen J, Howardy-Hansen P, Chraemmer-Jørgensen B, et al. Posttetanic Count (PTC): a new method of evaluating an intense nondepolarizing block. *Anesthesiology.* 1981;55:458–461.

B.11. What function does the conventional peripheral nerve stimulator (PNS) serve?

Since subjective estimates of the TOF ratio are so unreliable, one may ask whether intra-operative TOF stimulation serve any purpose. The answer is a resounding yes. The TOFC (the number of evoked responses at the thumb that can be detected) gives a useful estimate of the depth of neuromuscular block. A rough rule of thumb (no pun) follows: A TOFC of 1 equals T1 5% recovery, TOFC of 2 = 15% recovery, TOFC of 3 = 25% recovery, TOFC of 4 (with fade) ≧ 35% recovery. This information allows the clinician to judge the need for additional increments of blocking drug and the point in time when antagonism of residual block with an anticholinesterase is likely to be effective.

Kopman AF. Tactile evaluation of TOF count as an indicator of reliability of antagonism from vecuronium or atracurium-induced neuromuscular blockade. *Anesthesiology*. 1991;75:588–593.

B.12. How can the TOF ratio be measured quantitatively?

Prior to the current decade, the vast bulk of clinical research on neuromuscular function was done by measuring either evoked mechanical force (MMG) or summated electrical action potentials (EMG) at the adductor pollicis. While these techniques represent gold standards for reliability, they are unfortunately cumbersome to use in daily practice. In addition, at present, there are no commercially available MMG or EMG monitors designed for use in the operating room. However, using a different method of measurement (AMG), it is now possible to obtain a real-time display of the TOF ratio using a small handheld device,[1] which is relatively easy to set up and has a user-friendly interface. The rationale for AMG is based on Newton's second law of motion that states that force is equal to mass times acceleration. Presumably, the mass of the thumb remains constant so that the acceleration is directly proportional to force. For measurement of acceleration, a piezoelectric ceramic wafer is fixed to the thumb. When an evoked mechanical response of the thumb is elicited, an electrical signal proportional to the acceleration is generated in the ceramic transducer. This signal can then be digitized, processed, and electronically displayed in real time. Thus, it is now finally possible for the clinician to accurately and easily determine the extent of neuromuscular block (the TOF ratio) in real time. An excellent review of the pros, cons, and limitations of AMG may be found in the following reference:

Claudius C, Viby-Mogensen J. Acceleromyography for use in scientific and clinical practice: a systematic review of the evidence. *Anesthesiology*. 2008;108:1117–1140.

B.13. What are the limitations of anticholinesterase antagonists?

Nondepolarizing neuromuscular block is competitive in nature. Molecules of an NMBA compete with molecules of Ach for access to nicotinic binding sites or receptors at the myoneural junction. The NMBA-receptor or Ach-receptor binding is very evanescent in duration (msec). Thus, the relative concentration of NMBA versus Ach determines which molecule is most likely to succeed in the contest for receptor access. Anticholinesterases such as neostigmine affect antagonism by preventing Ach degradation and thus increasing the concentration of Ach in the synaptic cleft. However, there is a ceiling to this effect. Once the cholinesterase enzyme is completely inhibited, the addition of additional neostigmine or edrophonium will have no further effect. In contrast, there is no limit to the concentration of NMBA that may exist at the receptor if excessive doses of relaxant are administered. In practical terms, the maximum depth of block that can be rapidly antagonized by anticholinesterases approximately corresponds to the reappearance of the fourth response to TOF stimulation. To achieve rapid (within 10 minutes) reversal to a TOF ratio of 0.7 in more than 87% of patients, three or four tactile responses should be present at the time of neostigmine administration. It was not possible within 30 minutes to achieve a TOF ratio of 0.9 in all patients, regardless of the number of tactile responses present at neostigmine administration.

[1]The TOF-Watch Monitor (Organon Teknika B.V., Boxtel, The Netherlands).

Beemer GH, Goonetilleke PH, Bkorksten AR, et al. The maximum depth of an atracurium neuromuscular block antagonized by edrophonium to effect adequate recovery. *Anesthesiology*. 1995;82:852–858.

Kirkegaard H, Heier T, Caldwell JE. Efficacy of tactile-guided reversal from cisatracurium-induced neuromuscular block. *Anesthesiology*. 2002;96:45–50.

B.14. Is there anything wrong with administering neostigmine when the TOF count (TOFC) is less than 3?

As noted previously, when the TOFC is only 1 or 2, anticholinesterases cannot be counted on to achieve satisfactory reversal in a timely manner. The peak effect of the antagonist is followed by a plateau phase that represents the balance between diminishing anticholinesterase activity and spontaneous recovery. The latter becomes the major determinant at profound levels of neuromuscular block. However, even at a TOFC of 1 to 2, it may be possible to achieve a TOF ratio >0.40 within 10 minutes. The problem for the clinician is that further recovery may be quite slow, and unless an objective monitor of neuromuscular function is being used, the clinician is likely to have the false impression that adequate recovery has been achieved.

Kopman AF, Kopman DJ, Ng J, et al. Antagonism of profound cisatracurium and rocuronium block: the role of objective assessment of neuromuscular function. *J Clin Anesth*. 2005;17:30–35.

B.15. Is reversal of residual block always necessary?

If a quantitative monitor of neuromuscular function is used, the answer to this question is simple. If the TOF ratio approximates a value of 0.90 or better, anticholinesterase administration is pointless and is best avoided. Neostigmine, edrophonium, atropine, and so on all have their own side effects and should not be administered unnecessarily. Similarly, if the TOFC is less than 4 or 4 with obvious fade, then anticholinesterase administration is indicated. However, objective monitors are still not widely available. What should be done when the TOFC is 4 with no detectable fade?

Many clinicians base the decision of whether to reverse or not on the time interval since the last dose of relaxant. Unfortunately, this is often an unreliable way to proceed. Two hours after a single dose on an intermediate-duration blocker, 30% of individuals may have TOF ratios <0.90 and 10% will still not have returned to a value of 0.70.

Therefore, in the absence of objective evidence that the TOF ratio is >0.85 to 0.90, an antagonist should be administered. However, when no fade to TOF stimulation can be subjectively detected, the dose of neostigmine can be safely reduced to only 0.02 mg/kg.

Caldwell JE. Reversal of residual neuromuscular block with neotigmine at one to four hours after a single intubating dose of vecuronium. *Anesth Analg*. 1995;80:1168–1174.

Fuchs-Buder T, Meistelman C, Alla F, et al. Antagonism of low degrees of atracurium-induced neuromuscular blockade. Dose-effect relationships for neostigmine. *Anesthesiology*. 2010;112:34–40.

B.16. Is there any way to rapidly antagonize profound nondepolarizing block?

Until recently, the answer to this question was no. A radically new approach to reversal now presents itself with the introduction of sugammadex. At the moment

(July, 2010), this drug is available in Europe and Japan but not yet in North America. Sugammadex is a gamma-cyclodextrin. It acts by strongly binding with monoquaternary amino-steroid blocking agents (rocuronium and vecuronium) and thus lowers the free plasma concentrations of these drugs, allowing the agents to diffuse away from the myoneural junction. (Note: sugammadex is not an effective antagonist of benzylisoquinoliniumbased relaxants such as cisatracurium.) To give just one example of its efficacy, rocuronium is given in a dose of 1.2 mg/kg. Five minutes later, sugammadex 12 mg/kg is administered. In less than 2 minutes, the TOF ratio returned to a value of 0.90.

Another line of attack to the problem of antagonizing deep neuromuscular block is to design a relaxant that can be chemically degraded at will in vivo. A still experimental nondepolarizing blocker of intermediate duration (CW002) is a good example of this approach. The drug is a benzylisoquinolinium fumarate diester and is inactivated by L-cysteine. In dogs, L-cysteine decreased the duration of action from 70 minutes to less than 5 minutes.

de Boer H, Driessen JJ, Marcus MA, et al. Reversal of rocuronium-induced (1.2 mg/kg) profound neuromuscular block by sugammadex: a multicenter, dose-finding and safety study. *Anesthesiology*. 2007;107:239–244.

Naguib M, Brull SJ. Sugammadex: a novel selective relaxant binding agent. *Expert Rev Clin Pharmacol*. 2009;2:37–53.

Savarese JJ, McGilvra JD, Sunaga H, et al. Rapid chemical antagonism of neuromuscular blockade by l-cysteine adduction to and inactivation of the olefinic (double-bonded) isoquinolinium diester compounds gantacurium (AV430A, CW 002, and CW 011). *Anesthesiology*. 2010;113:58–73.

C. Postoperative Management

C.1. What is the incidence of residual neuromuscular block in the PACU?

Numerous reports since 2000 make clear that even with agents of intermediate duration, undetected residual weakness in the postoperative period is not a rare event. Large studies from Europe where routine reversal with cholinesterase inhibitors were not administered, 20% to 40% of patients arrived in their PACU with TOF values <0.70.

As might be expected, when a TOF ratio of 0.90 is set as the standard of adequate antagonism, the incidence of post-operative residual neuromuscular block (PORB) approaches 40%. The incidence of PORB is highly variable from institution to institution and very dependent on individual practice patterns. Diligent intraoperative monitoring and routine antagonism of residual block can result in dramatic reductions in the incidence of PORB. In a study from France, between 1995 and 2004, quantitative measurement and reversal of neuromuscular block in the operating room of one institution increased from 2% to 60% and from 6% to 42%, respectively. During the same time, the incidence of residual neuromuscular block defined as a TOF ratio less than 0.9 decreased from 62% to 3%.

Unfortunately, the lessons vividly demonstrated by these authors are far from universally understood or applied. A recent survey of North American and European clinical practices indicates that even in the year 2009, 10% of clinicians rarely or never monitor neuromuscular function with even the simplest of PNS, and the routine administration of antagonists is even less common.

Baillard C, Clec'h C, Catineau J, et al. Postoperative residual neuromuscular block: a survey of management. *Br J Anaesth*. 2005;95:622–626.

Baillard C, Gehan G, Reboul-Marty J, et al. Residual curarization in the recovery room after vecuronium. *Br J Anaesth.* 2000;84:394–395.

Cammu G, De Witte J, De Veylder J, et al. Postoperative residual paralysis in outpatients versus inpatients. *Anesth Analg.* 2006;102:426–429.

Hayes AH, Mirakhur RK, Breslin DS, et al. Postoperative residual block after intermediate-acting neuromuscular blocking drugs. *Anaesthesia.* 2001;56:312–318.

Kim KS, Lew SH, Cho HY, et al. Residual paralysis induced by either vecuronium or rocuronium after reversal with pyridostigmine . *Anesth Analg.* 2002;95:1656–1660.

Naguib M, Kopman AF, Lien CA, et al. A survey of current neuromuscular practice in the United States and Europe. *Anesth Analg.* 2010;111:110–119.

C.2. Does undetected postoperative residual neuromuscular block have clinical consequences?

In North America WNI-YAO in excess of 20 million patients each year receive an anesthetic. The size of the subgroup that receives a nondepolarizing blocking agent is unknown but obviously still numbers in the millions. As indicated previously, the exact incidence of PORB probably varies greatly from institution to institution; nonetheless, even if it is as low as 5% overall (highly optimistic), the number of individuals who arrive in the PACU with suboptimal neuromuscular recovery is substantial. Nevertheless, outcome studies that suggest that this a major public health risk are few and far between, and few clinicians perceive residual block as an important safety issue. In truth, the majority of patients who arrive in the PACU with TOF ratios <0.90 do not experience complications. However, not all individuals are so fortunate. Undetected PORB is clearly associated with potentially adverse respiratory events and increased morbidity. A recent prospective case controlled study of critical respiratory events (episodes of hypoxia, signs of airway obstruction, need for reintubation, etc.) in a university hospital's PACU is instructive. Sixty-one patients with critical respiratory events were identified. Their mean TOF ratio as measured by AMG was 0.62. The TOF value in 42 matched controls was 0.98. The same authors in a separate study were also able to demonstrate a lower frequency of residual neuromuscular blockade in the PACU (4.5%) (TOF ratio ≤ 0.9) in cases where intraoperative AMG was employed compared with the cases where conventional PNS were used (30%). During transport to the PACU, fewer AMG patients developed arterial oxygen saturation values, measured by pulse oximetry, of less than 90% (0%) or airway obstruction (0%) compared with subjective monitoring (21.1% and 11.1%, respectively). The incidence, severity, and duration of hypoxemic events during the first 30 minutes of PACU admission were less in the AMG group (all $P < .0001$). These findings add credence to the hypothesis that incomplete neuromuscular recovery is an important contributing factor in the development of adverse respiratory events in the PACU.

Brull SJ, Murphy GS. Residual neuromuscular block: lessons unlearned. Part II: Methods to reduce the risk of residual neuromuscular blockade. *Anesth Analg.* 2010;111:129–140.

Murphy GS, Szokol JW, Marymount JH, et al. Residual neuromuscular blockade and critical respiratory events in the postanesthesia care unit. *Anesth Analg.* 2008;107:130–137.

Murphy GS, Szokol JW, Marymount JH, et al. Intraoperative acceleromyography monitoring reduces the risk of residual neuromuscular blockade and adverse respiratory events in the postanesthesia care unit. *Anesthesiology.* 2008;109:389–398.

Murphy GS, Brull SJ. Residual neuromuscular block: lessons unlearned. Part I: Definitions, incidence, and adverse physiologic effects of residual neuromuscular block. *Anesth Analg.* 2010;111:120–128.

CHAPTER 55

Burns

Michael Tjeuw

A 45-YEAR-OLD MAN

who was smoking in bed sustained 40% second- and third-degree burns over his face, neck, chest, and upper extremities. He had a history of hypertension, angina, and angioplasty of the right coronary artery 1 year ago. He has smoked three packs of cigarettes per day for 20 years and he drinks alcohol daily. He is scheduled for tangential excision of eschar on the third day. Blood pressure, 190/100 mm Hg; heart rate, 120 beats per minute; and weight, 110 kg.

A. Medical Disease and Differential Diagnosis

1. How do you classify the burn injury?
2. How do you express the extent of the burn injury?
3. Should the "rule of nines" be used in children?
4. What is the definition of a major burn according to the American Burn Association?
5. What functions does the skin perform?
6. What pathophysiologic changes accompany major thermal injury?
7. Name some of the known mediators released with thermal injury. What are the responses to those mediators?
8. What is the prognosis for this patient? What major factors affect his prognosis?
9. What are the most common causes of death?
10. Does this patient have a smoke inhalation burn? How do you make the diagnosis?
11. Could you name some of the chemical products of combustion?
12. What is carbon monoxide poisoning? How do you treat carbon monoxide poisoning?
13. What resuscitative measure would you institute immediately in this patient with 40% burns?
14. What fluid formula would you use?
15. What cardiovascular changes typify the burn injury?
16. Is the immune system affected in burn injury? How?

17. What hematologic changes occur in burn injury?
18. What changes occur in liver function? What are the anesthetic implications of such changes?
19. What are Curling ulcers? How can they be prevented?
20. What complications are associated with electrical burns?

B. Preoperative Evaluation and Preparation

1. What preoperative preparations would you order? What are particular concerns in this patient?
2. What are the various operative and management options available for severely burned patients?
3. What is tangential excision split-thickness skin graft (TE/STSG)? What are the principles of this grafting technique?
4. What are the advantages and disadvantages of early TE/STSG?
5. What is this patient's mean arterial blood pressure? How do you calculate it?
6. Are you concerned about this patient's blood pressure? What treatment would you institute?
7. This patient was ventilated with respirator settings of tidal volume 800 mL; respiratory rate, 20 breaths per minute; F_{IO_2}, 60%; and positive end-expiratory pressure, 10 cm H_2O. Arterial blood gas analyses showed the following: pH, 7.25; P_{O_2}, 56 mm Hg; P_{CO_2}, 60 mm Hg; and O_2 saturation, 80%. How would you interpret these arterial blood gas analysis results? What are the possible causes of high P_{CO_2} and low P_{O_2}?
8. How do you calculate oxygen content and oxygen delivery? What factors govern the oxygen delivery to the tissues? What are the causes of tissue hypoxia?
9. What are the symptoms and signs of alcohol withdrawal? Are you concerned that this patient could develop delirium tremens?
10. How would you prevent the adverse effects of alcohol withdrawal?

C. Intraoperative Management

1. What monitors would you use in the operating room?
2. What information can be obtained from an arterial line and a pulmonary artery catheter? How are these calculations performed?
3. If the patient had not been intubated, how would you proceed with the anesthetic induction?
4. Why is awake intubation considered the safest?
5. What anesthetic agents would you use? Discuss inhalation versus intravenous agents.
6. Why are you concerned about the patient's body temperature? What is normothermia for a burned patient?
7. How is temperature best maintained?
8. What derangements occur with hypothermia?
9. What muscle relaxant would you use?
10. Why is succinylcholine contraindicated in burned patients? For how long should it be avoided?
11. What other adverse effects are associated with succinylcholine?
12. How are the doses of nondepolarizing muscle relaxants affected by burn injury?
13. How are the muscle relaxants such as succinylcholine, atracurium, cisatracurium, vecuronium, pancuronium, rocuronium, and curare metabolized and eliminated? Which of them has significant histamine release?
14. What is the difference between metabolism and elimination of drugs?

D. Postoperative Management

1. How would you monitor this patient during transport?
2. What is meant by diffusion hypoxia? How do you prevent it?
3. Why do patients often shiver in the recovery room on emergence from anesthesia?
4. Discuss the causes of oliguria in the recovery room.

A. Medical Disease and Differential Diagnosis

A.1. How do you classify the burn injury?

Burns are classified as first, second, or third degree. First-degree, or superficial, burns are characterized by simple erythema of the skin, with only microscopic destruction of superficial layers of the epidermis. Second-degree, or partial-thickness, burns extend through the epidermis into the dermis. Even when most of the epithelium is destroyed, regeneration may occur from epithelial cells surrounding hair follicles or sweat glands. Third-degree, or full-thickness, burns are characterized by total, irreversible destruction of all the skin, dermal appendages, and epithelial elements. Spontaneous regeneration of epithelium is not possible and the burns are described as full-thickness burns. Such burns require the application of skin grafts if the development of scar tissue is to be avoided. Fourth-degree burns refer to deep thermal injuries involving fascia, muscle, or bone (Table 55.1).

Brunicardi FC, Anderson DK, eds. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:199–200.

MacLennan N, Heimbach DM, Cullen BF. Anaesthesia for major thermal injury. *Anesthesiology*. 1998;89:749–770.

Table 55.1 Classification of Burn Depth

CLASSIFICATION	BURN DEPTH	OUTCOME
Superficial		
First degree	Confined to epidermis	Heals spontaneously
Partial thickness		
Second degree		
Superficial dermal burn	Epidermis and upper dermis	Heals spontaneously
Deep dermal burn	Epidermis and deep dermis	Requires excision and grafting for rapid return of function
Full thickness		
Third degree	Destruction of epidermis and dermis	Wound excision and grafting required Some limitation of function and scar formation
Fourth degree	Muscle, fascia, bone	Complete excision required, limited function

From MacLennan N, Heimbach DM, Cullen BF. Anesthesia for major thermal injury. *Anesthesiology.* 1998;89:749–779, with permission.

A.2. How do you express the extent of the burn injury?

The extent of the burn injury is expressed as a percentage of the total body surface area (TBSA) displaying either second- or third-degree burns. It is most commonly estimated by the "rule of nines" (Fig. 55.1). The major anatomic portions of the adult may be divided into multiples of 9% of the body surface area. The proportion of each of these areas is estimated and the sum represents the percentage of the TBSA burn. The percentages of body surface are as follows:

- Head and neck 9%
- Right upper extremity 9%
- Left upper extremity 9%
- Right lower extremity 18%
- Left lower extremity 18%
- Anterior trunk 18%
- Posterior trunk 18%
- Perineum 1%

Brunicardi FC, Anderson DK, eds. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:199–200.

MacLennan N, Heimbach DM, Cullen BF. Anesthesia for major thermal injury. *Anesthesiology*. 1998;89:749–770.

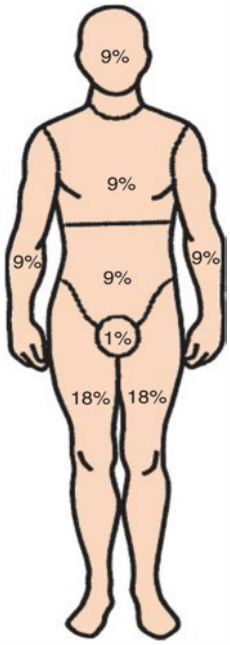


Figure 55.1 The rule of nines for determining the percentage of body surface area burned in adults. (Adapted from MacLennan N, Heimbach DM, Cullen BF. Anesthesia for major thermal injury. *Anesthesiology*. 1998;89:749–770.)

A.3. Should the "rule of nines" be used in children?

The "rule of nines" may not be used to estimate TBSA burns in children because the surface area of the head and neck in children is significantly larger than 9%, and that of the lower extremities is smaller. More precise methods, such as the Lund and Browder chart, may be used to provide greater accuracy by taking into account the changing proportions of the body from infancy to adulthood (Fig. 55.2).

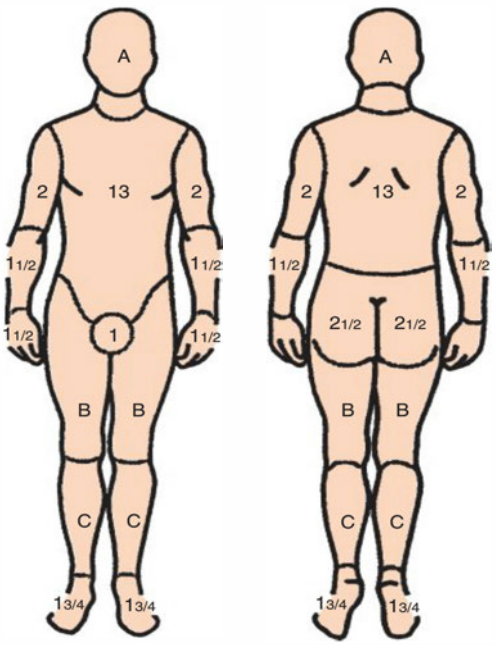
Brunicardi FC, Anderson DK, eds. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:199–200.

MacLennan N, Heimbach DM, Cullen BF. Anesthesia for major thermal injury. *Anesthesiology*. 1998;89:749–770.

A.4. What is the definition of a major burn according to the American Burn Association?

The American Burn Association defines a major burn as follows:

- Full-thickness burns more than 10% TBSA
- Partial-thickness burns more than 25% in adults or 20% at extremes of age
- Burns involving face, hands, feet, or perineum
- Inhalation, chemical, or electrical burns
- Burns in patients with serious pre-existing medical disorders (adapted from the American Burn Association injury severity grading system)



Relative percentages of areas affected by growth

	AGE IN YEARS					
AREA	0	1	5	10	15	Adult
A: half of head	9½	8½	6½	5½	4½	3½
B: half of thigh	2¾	3¼	4	4¼	4½	4¾
C: half of leg	2½	2½	2¾	3	3¼	3½

Figure 55.2 Diagram and table for determining the percentage of body surface area burned in children. (Adapted from MacLennan N, Heimbach DM, Cullen BF. Anesthesia for major thermal injury. *Anesthesiology*. 1998;89:749–770.)

A.5. What functions does the skin perform?

The skin is the largest organ of the body, with surface area ranging from 1.5 to 2.0 m^2 in the adult. It protects the invasion of microorganisms. It performs other functions in thermal regulation, fluid and electrolytes homeostasis, and sensation (touch, temperature, pain). The skin also has metabolic functions including vitamin D metabolism.

Herndon DN, ed. *Total Burn Care*. 3rd ed. Philadelphia: Saunders-Elsevier; 2007:239–240.

A.6. What pathophysiologic changes accompany major thermal injury?

The pathophysiologic alterations that accompany major thermal injury are complex. When destroyed, skin, which is the largest organ of the body, has a systemic impact. Thermal regulation, fluid and electrolyte homeostasis, and protection against bacterial infection are affected. Immediately after a burn injury, mediators released from the burn wound contribute to local inflammation and edema. A large amount of fluid is lost from the vascular compartment into the burn wound. Sequestration in the extravascular space results in significant hemoconcentration. Increased secretion of antidiuretic hormone may decrease or even completely inhibit urinary output. It has been shown that during the first 4 days after a burn, an amount of albumin equal to twice the total plasma albumin content is lost through the wound. Half of this fluid remains sequestered in the extravascular space for 3 weeks or more before returning to the intravascular compartment.

The metabolic rate is markedly increased after the burn injury. Depending on the size of the burn, the increase in metabolic rate can be doubled or tripled with a proportionate increase in oxygen consumption and carbon dioxide production. This hypermetabolic state will continue for weeks or months until full skin coverage is achieved and the tissue repair processes are complete. Cardiac output (CO) is often decreased in patients with major burns. This decrease is not entirely explained by the rapid reduction in circulating blood volume. It has been shown that a circulating myocardial-depressant factor exists in both humans and laboratory animals.

Changes in vascular integrity occur in other areas remote from the injury site. The entire vascular compartment in the body becomes permeable to circulating macromolecules, such as dextran. This capillary leak syndrome is manifested as edema. In the lung, severe pulmonary edema can be life threatening.

Pulmonary function decreases markedly. Functional residual capacity is reduced. Both lung compliance and chest wall compliance decrease markedly. The alveolar–arterial oxygen gradient (P_{AO_2}–Pa_{O_2}) increases. Minute ventilation is increased; it can be as high as 40 L per minute (normal, 6 L per minute).

Brunicardi FC, Anderson DK, eds. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:197–205.

Herndon DN, ed. *Total Burn Care*. 3rd ed. Philadelphia: Saunders-Elsevier; 2007:93–97.

MacLennan N, Heimbach DM, Cullen BF. Anesthesia for major thermal injury. *Anesthesiology*. 1998;89:749–770.

A.7. Name some of the known mediators released with thermal injury? What are the responses to those mediators?

After a thermal injury, mediators released from the burn wound contribute to local inflammation and edema. Local mediators include histamine, prostaglandins,

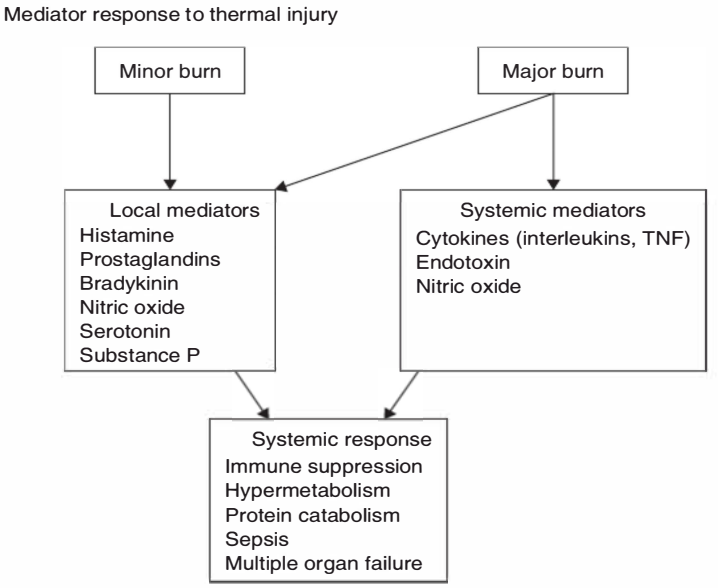


Figure 55.3 Mediators released with thermal injury and the response to their release. TNF, tumor necrosis factor. (From MacLennan N, Heimbach DM, Cullen BF. Anesthesia for major thermal injury. *Anesthesiology.* 1998;89:749–770, with permission.)

thromboxane, bradykinin, nitric oxide, serotonin, catecholamine, and platelet aggregation factor.

In minor burns, the inflammatory process is limited to the wound itself. In major burns, local injury triggers the release of circulating (systemic) mediators, resulting in a systemic response. This is characterized by hypermetabolism, immune suppression, and the systemic inflammatory response syndrome (protein catabolism, sepsis, multiple organ failures).

The systemic mediators are cytokines (interleukins), endotoxin, and nitric oxide (Fig. 55.3).

Brunicardi FC, Anderson DK, eds. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:197–205.

Herndon DN, ed. *Total Burn Care*. 3rd ed. Philadelphia: Saunders-Elsevier; 2007:97–99.

MacLennan N, Heimbach DM, Cullen BF. Anesthesia for major thermal injury. *Anesthesiology*. 1998;89:749–770.

A.8. What is the prognosis for this patient? What major factors affect his prognosis?

The prognosis for this patient is very poor. Statistical survival based on TBSA alone would predict a less than 50% chance of survival. Other factors that affect his prognosis are age, size and depth of burn, associated pulmonary injury, and pre-existing medical disease. In view of this patient, who had angioplasty for coronary artery disease and hypertension and who is a heavy smoker and obese, the risk of myocardial infarction is greatly increased.

A.9. What are the most common causes of death?

With the understanding of vigorous early fluid resuscitation, hypovolemic shock is not common in United States. The major early cause of death is asphyxia. The most common cause of long-term mortality is septic complications.

A.10. Does this patient have a smoke inhalation burn? How do you make the diagnosis?

The patient probably sustained a smoke inhalation burn. Smoke inhalation should be highly suspected in patients who were burned in an enclosed space, received burns of the face, were burned while under the influence of alcohol or drugs, or lost consciousness at the time of the accident.

A patient with smoke inhalation often exhibits no physical signs or symptoms during the first 24 hours after the burn. Diagnosis is dependent on a high index of suspicion and careful physical and laboratory examination. The early symptoms and signs of respiratory tract injury include singed nasal hair; burned nasal mucosa, lips, and mouth; hoarseness; wheezing; and brassy cough with soot in the sputum. The posterior pharynx may appear red and the larynx may appear edematous. Radiographic findings are usually negative immediately after injury; this is the "clear or lucid period." Laboratory tests include blood gas analysis, carboxyhemoglobin concentration, xenon scans, and fiber-optic bronchoscopy.

Brunicardi FC, Anderson DK, eds. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:201–202.

Herndon DN, ed. *Total Burn Care*. 3rd ed. Philadelphia: Saunders-Elsevier; 2007:262–265.

A.11. Could you name some of the chemical products of combustion?

Carbon monoxide is produced by incomplete combustion of carbon-containing compounds such as wood, coal, and gasoline. Other chemical products of combustion include ammonia, cyanide, hydrogen chloride, sulfur dioxide, and phosgene. These chemicals combine with water to produce strong acids and alkalines.

Herndon DN, ed. *Total Burn Care*. 3rd ed. Philadelphia: Saunders-Elsevier; 2007:248–250.

A.12. What is carbon monoxide poisoning? How do you treat carbon monoxide poisoning?

Carbon monoxide is the leading cause of hypoxia in survivors of burn injuries. Carbon monoxide has a 200 times greater affinity for hemoglobin than oxygen and therefore displaces oxygen from its hemoglobin-binding sites. Fortunately, this reaction is a competitive, reversible one, so oxygen therapy should be instituted immediately. The half-life for carbon monoxide elimination from hemoglobin can be shortened from 4 hours to 45 minutes with an inspired oxygen concentration of 100%. Although the Pa_{O_2} may be normal, the actual content of oxygen in the blood is markedly reduced.

Brunicardi FC, Anderson DK, eds. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:201–202.

Herndon DN, ed. *Total Burn Care*. 3rd ed. Philadelphia: Saunders-Elsevier; 2007:250–256.

A.13. What resuscitative measure would you institute immediately in this patient with 40% burns?

Vigorous fluid resuscitation should be instituted immediately to combat the danger of hypovolemia from translocation of intravascular volume into the burn edema, which acts as a "third space." Fluid must be administered adequately to ensure good tissue perfusion and adequate urine output. The airway should be maintained to ensure adequate ventilation. If an upper airway burn is involved, endotracheal intubation is indicated.

A.14. What fluid formula would you use?

Over the last 30 years, many fluid formulas have been developed as guides to initial resuscitation in hypovolemic shock after burn injury. Most use various combinations of crystalloid and colloid solutions, but they differ widely in the colloid/crystalloid ratio and in the rate of fluid administration. Although much controversy still surrounds the use of "the solution" for resuscitation in burn shock, scientific investigation supports the need for both crystalloid and colloid solutions (Table 55.2). Which formula is used to begin such therapy matters little, as long as it is modified according to the patient's changing requirements. The Parkland formula, popularized by Baxter, has been adopted in most burn centers because of its simplicity, reduced cost, and equivalent outcome and is currently the standard against which new formulas must be compared.

Parkland formula

First 24 hours

- *Electrolyte solution (lactated Ringer's)*. 4 mL/kg/percentage of body area with second- and third-degree burn
- *Administration rate*. Half the solution given in the first 8 hours, one-quarter in the second 8 hours, one-quarter in the third 8 hours
- *Urine output*. Maintain at 0.5 to 1.0 mL/kg/hour

Second 24 hours

- *Glucose in water*. To replace evaporated water loss and maintain serum sodium concentration of 140 mEq per L

Table 55.2 Fluid Resuscitation for Adults with Major Burns

Crystalloid Regimens		
Parkland	Lactated Ringer's	4 mL/kg/% burn
Modified Brooke	Lactated Ringer's	2 mL/kg/% burn
Colloid regimens		
Evans	Normal saline	1 mL/kg/% burn
	Colloid	1 mL/kg/% burn
	5% Dextrose	2,000 mL/24 hr
Brooke	Lactated Ringer's	1.5 mL/kg/% burn
	Colloid	0.5 mL/kg/% burn
	5% Dextrose	2,000 mL/24 hr

- *Colloid solutions (e.g., albumin)*. Amount proportional to burn
  - *30% to 50% burn*: 0.3 mL/kg/percentage of burn
  - *50% to 70% burn*: 0.4 mL/kg/percentage of burn
  - *Larger than 70% burn*: 0.5 mL/kg/percentage of burn
- *Urine output*. Maintain at 0.5 to 1.0 mL/kg/hour

Brunicardi FC, Anderson DK, eds. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:199–201.

Herndon DN, ed. *Total Burn Care*. 3rd ed. Philadelphia: Saunders-Elsevier; 2007:201–204.

A.15. What cardiovascular changes typify the burn injury?

Cardiovascular changes develop in several phases. Acutely, fluid sequestration in the burned area and from capillary leak is caused by direct thermal destruction of the capillary membranes. This results in a massive shift of fluids and proteins from the intravascular compartment to the interstitial spaces. This shift of fluid accounts for the marked decrease in circulating blood volume, resulting in hypotension or the initial burn shock. Decreased blood volume and decreased CO would trigger catecholamine release, resulting in severe vasoconstriction, which may further compromise forward flow and tissue perfusion. Release of myocardial-depressant factors may further depress CO through its direct action on myocardial contractility.

Brunicardi FC, Anderson DK, eds. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:197–205.

Hendon DN, ed. *Total Burn Care*. 3rd ed. Philadelphia: Saunders-Elsevier; 2007:471–472.

A.16. Is the immune system affected in burn injury? How?

Both the cellular and the humoral components of the immune system are impaired. The presence of devitalized tissue greatly increases the risk of wound infection and systemic sepsis. Endotoxins cause changes in cellular function. Macrophage activity in the alveolar is impaired. Changes in phagocytic and chemotactic properties of neutrophils have been demonstrated. Strict antiseptic precautions must be observed in these patients.

Brunicardi FC, Anderson DK, eds. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:197–205.

Herndon DN, ed. *Total Burn Care*. 3rd ed. Philadelphia: Saunders-Elsevier; 2007:310–324.

A.17. What hematologic changes occur in burn injury?

Hematologic changes can be seen in erythrocytes (red blood cells [RBCs]), platelets, and the coagulation mechanism.

Erythrocytes (RBCs). Immediately after injury, the hematocrit level increases as noncellular fluid translocates into the interstitium. Anemia is more often the case after fluid resuscitation because of RBC damage and hemolysis during the heating injury. There is shortened RBC half-life and reduction of production due to circulating inhibitory factors.

Platelets. The platelet count usually decreases because of dilutional and consumption by formation of microaggregates in the skin and smoke damaged lung. The platelet level returns to normal by the end of the first week unless sepsis or multiple system organ failure occurs.

Coagulation. Both the thrombotic and the fibrinolytic mechanisms are activated, and clotting factors decrease. Disseminated intravascular coagulopathy is rare but can occur, particularly in fourth-degree burns involving structures deep to the skin.

Brunicardi FC, Anderson DK, eds. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:197–205.

Herndon DN, ed. *Total Burn Care*. 3rd ed. Philadelphia: Saunders-Elsevier; 2007:325–327.

A.18. What changes occur in liver function? What are the anesthetic implications of such changes?

Hypoperfusion during burn shock can result in decreased hepatic function, severely depressing the detoxification capacity of the liver. Decreased levels of albumin may result in greater free fractions of bound drugs such as benzodiazepines and phenytoin. In contrast, the injury-stimulated rise in the acute-phase reactant α_1-acid-glycoprotein increases the binding of basic drugs such as muscle relaxants, lidocaine, and propranolol.

Brunicardi FC, Anderson DK, eds. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:197–205.

Herndon DN, ed. *Total Burn Care*. 3rd ed. Philadelphia: Saunders-Elsevier; 2007:361–375.

Martyn JAJ. The use of neuromuscular relaxants in burn patients. In: Rupp SM, ed. *Problems in Anesthesia*. Philadelphia: JB Lippincott; 1989:482.

A.19. What are Curling ulcers? How can they be prevented?

Curling ulcer is a stress ulcer of the duodenum commonly found after a severe burn. Gastric ulceration may occur also. Without treatment, the incidence is as high as 80%. The frequency and severity correlate with the size of the burn. They may present with gastric bleeding. They can be prevented with prophylactic antacids, H_2-antagonists, and early enteral feeding.

Brunicardi FC, Anderson DK, eds. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:910.

Herndon DN, ed. *Total Burn Care*. 3rd ed. Philadelphia: Saunders-Elsevier; 2007:472.

A.20. What complications are associated with electrical burns?

The burn from electrical current results from the conversion of electrical energy to thermal energy. The damages may vary and are determined by the area of contact, the resistances of the tissues, and the duration of current flow. Often, only the surface entrance and exit sites on the skin show visible injury because of the high current concentrations at these points. Deep tissues such as muscles, tendons, blood vessels, and nerves can be severely injured. Vascular complications such as thrombosis can be late complications. The heart is particularly susceptible to electrical damage. Ectopy and congestive heart failure can be signs of electrical injury.

B. Preoperative Evaluation and Preparation

B.1. What preoperative preparations would you order? What are particular concerns in this patient?

Preoperative preparations should include a medical history, physical examination, and the usual concerns regarding cardiac disease, pulmonary disease, renal function, liver function, anesthetic history, and family history. Of particular concern in this patient are hypertension, ischemic heart disease, angioplasty of left main coronary artery, and the history of heavy smoking and heavy alcohol consumption.

The adequacy of fluid volume resuscitation should be assessed.

Hemodynamic stability should have been achieved.

Laboratory tests should include complete blood cell count, platelet count, electrolytes, blood urea nitrogen, creatinine, coagulation studies, urinalysis, liver function test, electrocardiogram (ECG), chest radiograph, and arterial and venous blood gases.

Other data that may be helpful include central venous pressure (CVP), pulmonary artery occlusion pressure (PAOP), CO, and cardiac index (CI).

In view of this patient's left main coronary artery disease, cardiac enzymes studies in conjunction with cardiologist involvement would be beneficial.

B.2. What are the various operative and management options available for severely burned patients?

Deep partial-thickness and full-thickness burns will not heal spontaneously and require excision and skin graft. The burned skin or eschar is a good culture medium for bacterial growth. Although topical antibiotic creams such as silver sulfadiazine can be applied to control the infection, the definitive treatment is excision of eschar.

The timing and extent of burn wound excision are still debatable; there has been a shift toward earlier excision and grafting. The most widely used approach involves an initial 48-hour period of stabilization, followed by tangential excision split-thickness skin graft (TE/STSG). The extent of excision is limited to 20%. These procedures are repeated every 2 days until the eschar excision is complete. Some favor very early excision (<24 hours from the time of burn).

Brunicardi FC, Anderson DK, eds. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:197–205.

Herndon DN, ed. *Total Burn Care*. 3rd ed. Philadelphia: Saunders-Elsevier; 2007:177–187.

B.3. What is tangential excision split-thickness skin graft (TE/STSG)? What are the principles of this grafting technique?

TE/STSG is a procedure to debride the dead skin and graft on new layers. The burn eschar is sharply excised from the underlying subcutaneous tissue. Brisk capillary bleeding signifies that adequate excision has been achieved and viable tissue uncovered. Skin grafts may be either full thickness or split (partial) thickness. Full-thickness grafts include all layers of epidermis and dermis in their sample. Therefore, the donor site must be closed primarily. Suitable donor sites are the skinfolds of the axilla and groin. A tissue expander is commonly used to increase the available donor skin. Full-thickness grafts have the advantage of better cosmesis and durability, and they are useful when tissue bulk is desired. More commonly, STSGs are used. These grafts are obtained by slicing the superficial layers of the skin through the level of the dermal pegs. Because maturation of skin cells occurs as they migrate superficially, the graft has many viable layers of dermal cells. When placed on a viable bed of subcutaneous tissue, ingrowth of vessels occurs and the graft remains viable. In addition, because the

excision of donor skin is through the dermis, the deep basement membrane and skin appendages remain intact. Hence, the donor site will heal on its own, architecturally normal, usually with only mild discoloration.

Brunicardi FC, Anderson DK, eds. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:179–184.

Herndon DN, ed. *Total Burn Care*. 3rd ed. Philadelphia: Saunders-Elsevier; 2007:197–205.

B.4. What are the advantages and disadvantages of early TE/STSG?

By excising the burn eschar early (within 7 to 10 days), one can remove the bacterial load quickly and achieve prompt skin coverage with resultant lessening of septic complications; the hospital and recovery phases are therefore shortened. Very early excision (within 24 hours), however, has the disadvantage of the patient undergoing a major operation during the resuscitative phase of the injury. The patient is not optimally stabilized, and there is an increase in anesthetic risk.

Cultured epithelial autografts are an exacting new technique that can be of great use in patients with large TBSA burns in which donor sites are few in number.

Brunicardi FC, Anderson DK, eds. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:197–205.

Herndon DN, ed. *Total Burn Care*. 3rd ed. Philadelphia: Saunders-Elsevier; 2007:177–187.

Munster AM, Weiner SH, Spence RJ. Cultured epidermis for the coverage of massive burn wounds: a single center experience. *Ann Surg*. 1990;211:676–680.

B.5. What is this patient's mean arterial blood pressure? How do you calculate it?

The patient's blood pressure is 190/100 mm Hg; therefore, his mean arterial blood pressure is 130 mm Hg (mean arterial pressure = diastolic pressure + one-third of pulse pressure, which is the difference between systolic and diastolic pressure).

B.6. Are you concerned about this patient's blood pressure? What treatment would you institute?

The blood pressure is quite high (190/100 mm Hg). Knowing that this patient has a history of ischemic heart disease with symptoms of angina that required angioplasty of the left main coronary artery 1 year ago, I am very concerned about his hypertension and would like to control the blood pressure to the normal range.

The following intravenous vasodilators may be used:

- Beta-blockers (intravenous labetalol, lopressor)
  - calcium channel blocker (intravenous infusion of nicardipine or clavidipine)
  - angiotensin-converting enzyme inhibitors (intravenous Vasotec)
- Hydralazine

In view of his tachycardia (heart rate, 120 beats per minute), I would prefer an intravenous beta-blocker such as labetalol or lopressor. Increased afterload and tachycardia would increase oxygen demand on the heart and increase the risk of myocardial infarction.

Adequate volume resuscitation should be assessed, so obtaining CVP, PAOP, CO, CI, and systemic vascular resistance would be helpful in instituting treatment.

B.7. This patient was ventilated with respirator settings of tidal volume, 800 mL; respiratory rate, 20 breaths per minute; F_{IO_2}, 60%; and positive end-expiratory pressure, 10 cm H_2O. Arterial blood gas analyses showed the following: pH, 7.25; P_{O_2}, 56 mm Hg; P_{CO_2}, 60 mm Hg; and O_2 saturation, 80%. How would you interpret these arterial blood gas analysis results? What are the possible causes of high P_{CO_2} and low P_{O_2}?

Arterial blood gas analysis results are abnormal. This patient was hypoventilated with high P_{CO_2} of 60 mm Hg (normal P_{CO_2} is 35 to 45 mm Hg); although the minute volume was 16 L (800 mL × 20), the increase in minute volume might not have compensated for his hypermetabolic state with marked increase in CO_2 production.

Ventilation/perfusion mismatch is the most common cause of hypoxemia. Causes of ventilation/perfusion mismatches range from dead space to shunt. The common causes are atelectasis, pneumonia, and pulmonary edema.

This patient had respiratory acidosis and probably mild metabolic acidosis.

Malposition of endotracheal tube with single-lung ventilation is a possible cause that should be ruled out.

B.8. How do you calculate oxygen content and oxygen delivery? What factors govern the oxygen delivery to the tissues? What are the causes of tissue hypoxia?

Oxygen content consists of oxygen in combination with hemoglobin and oxygen dissolved in plasma and can be expressed as:

$$\text{Oxygen content (mL/dL)} = 1.31 \times \text{hemoglobin (g/dL)} \times O_2 \text{ saturation (\%)} + 0.003 \times P_{O_2}$$

Normal arterial oxygen content: $Ca_{O_2} = 20.73$ mL per 100 mL

Normal venous oxygen content: $C_vo_2 = 15.76$ mL per 100 mL

Oxygen delivery is the product of cardiac output (CO) and arterial oxygen content.

$$Do2 = CO \times Ca_{O_2} = CO \times ([1.31 \times \text{hemoglobin} \times O_2 \text{ saturation}] + 0.003 \times P_{O_2})$$

Three main factors govern the oxygen delivery: CO, hemoglobin, and arterial oxygen saturation.

Tissue hypoxia may be due to the following:

- Inadequate CO: "stagnant anoxia"
- Inadequate arterial oxygen saturation: "anoxic anoxia"
- Reduction of hemoglobin concentration: "anemic anoxia"

Lumb AB. *Nunn's Applied Respiratory Physiology*. 6th ed. Philadelphia: Butterworth-Heinemann; 2005:188.

B.9. What are the symptoms and signs of alcohol withdrawal? Are you concerned that this patient could develop delirium tremens?

Minor withdrawal symptoms are anorexia, insomnia, tremors, mild disorientation, hallucination, and convulsion. These symptoms usually peak within 10 to 30 hours of cessation of drinking. Major withdrawal symptoms occur later and are characterized by severe autonomic hyperactivity, which includes anxiety, tachycardia, diaphoresis,

tremors, fever, hallucination, and global convulsion. These major symptoms are also known as *delirium tremens*. There is a real concern that this patient could develop withdrawal syndrome. Early treatment should be instituted.

B.10. How would you prevent the adverse effects of alcohol withdrawal?

Sedatives, such as benzodiazepines, are effective in preventing the withdrawal symptoms. If autonomic hyperactivity symptoms occur, beta-blockers are helpful to attenuate the symptoms, especially tachycardia and dysrhythmias.

C. Intraoperative Management

C.1. What monitors would you use in the operating room?

The routinely used monitors, such as ECG, blood pressure, temperature, inspired oxygen, pulse oximetry, and capnography, should be used in this patient. A urinary catheter is essential to assess urine output. An indwelling arterial line is helpful, because a standard blood pressure cuff would be difficult to apply over the areas to be grafted and harvested. A pulmonary artery catheter or CVP catheter is recommended for the severely burned patient, especially a patient with ischemic heart disease.

C.2. What information can be obtained from an arterial line and a pulmonary artery catheter? How are these calculations performed?

The arterial line can display direct continuous blood pressure, thereby providing continuous real-time monitoring of blood pressure. This is most useful in fluctuating hypotensive or hypertensive situations. In conditions such as atrial fibrillation or ventricular tachycardia, variations in ventricular response or blood pressure can be recognized instantly. The morphology of the waveform can also provide information about arterial resistance (narrow suggestive of both reduced stroke volume and increased systemic vascular resistance) stroke volume (area under the curve), and preload (pulse pressure variation particularly in response to mechanical positive pressure ventilation). In addition, it serves as ready vascular access for blood sampling—for example, arterial blood gas analyses, electrolytes, hematocrit, and blood sugar levels.

Pulmonary artery catheter allows measurement of PAOP. The PAOP is a surrogate of left atrial pressures. Left atrial pressure reflects left ventricular end-diastolic pressure, which is helpful in assessing the preload status of the left ventricle. CVP, although useful as a rough estimate of preload, does not correlate with left ventricular end-diastolic pressure when either isolated right-sided or left-sided cardiac dysfunction occurs.

The multilumen pulmonary artery catheters are capable of measuring CVP and CO through the thermodilution method. It also permits sampling of mixed venous blood. These measurements permit calculation of many hemodynamic variables.

$$\text{Cardiac index (CI)} = \frac{\text{CO}}{\text{Body surface area}} \qquad \text{(normal 2.8 to 4.2 L/min/m}^2\text{)}$$

$$\text{Stroke volume (SV)} = \frac{\text{CO}}{\text{Heart rate}} \qquad \text{(normal 60 – 80 mL/beat)}$$

$$\text{Stroke index (SI)} = \frac{\text{CI}}{\text{Heart rate}} \qquad \text{(normal 40 – 65 mL/beat/m}^2\text{)}$$

$$\text{Systematic vascular resistance (SVR)} = \frac{\text{Mean BP} - \text{CVP}}{\text{CO}} \times 80 \qquad \text{(normal 900 – 1,400 dynes/sec/cm}^5\text{)}$$

$$\text{Pulmonary vascular resistance (PVR)} = \frac{\text{Mean PAP} - \text{PCWP}}{\text{CO}} \times 80 \quad \text{(normal 150 – 250 dynes/sec/cm}^5\text{)}$$

Mixed venous blood samples are needed for shunt calculations:

$$\frac{\dot{Q}_s}{\dot{Q}_t} = \frac{Cc\bar{v}o_2 - Cao_2}{Cc\bar{v}o_2 - C\bar{v}\bar{v}o_2}$$

$Cc\bar{v}o_2$ = pulmonary capillary oxygen content
Cao_2 = artery oxygen content
$C\bar{v}\bar{v}o_2$ = mixed venous oxygen content

A low mixed venous oxygen level (<30 mm Hg) is suggestive of inadequate tissue perfusion.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier/Churchill Livingstone; 2010:1317, 1414.

C.3. If the patient had not been intubated, how would you proceed with the anesthetic induction?

One should anticipate a difficult intubation because this patient has burns over his face and neck. Burns on the face may cause severe edema of the face, pharynx, and larynx, so careful assessment of the mouth opening, pharynx, and larynx should be performed. The safest way to secure the airway is to do an awake intubation with topical anesthesia and mild sedation; it can be achieved with either direct or fiber-optic–guided intubation. If prolonged postoperative intubation is anticipated, the nasotracheal route should be considered. A nasotracheal tube is more easily secured in place, is better tolerated by the patient, and permits better oral hygienic care. Vasoconstriction of the nasal mucosa may be achieved with phenylephrine drops.Alternatively, a tracheostomy should be considered early in those patients with acute lung injury who will require prolonged mechanical ventilation.

C.4. Why is awake intubation considered the safest?

Awake intubation is considered the safest way to secure an airway because when the patient is awake and breathing spontaneously, the patient is less likely to obstruct the upper airway by the tongue and is less likely to have oxygen desaturation. The anesthesiologist does not have to ventilate using a mask and is therefore less likely to distend the stomach.

If the patient is breathing spontaneously and has adequate oxygenation, the anesthesiologist has more time to do a proper laryngoscopy or manipulation of the endotracheal tube. Identifying the passage of air from the glottis may be helpful in blind intubation.

C.5. What anesthetic agents would you use? Discuss inhalation versus intravenous agents.

For the severely burned patient, once the airway is secured, high-dose narcotic-muscle relaxant technique would be preferred, because this technique offers good intraoperative hemodynamic stability in critically ill patients, coupled with excellent postoperative analgesia.

The narcotics such as morphine, meperidine (Demerol), fentanyl, or sufentanil can be used because they do not depress myocardial contractility, whereas potent inhalation agents depress the myocardium. If inhalation agents are chosen, the concentration should be carefully titrated to prevent loss of cardiovascular compensation.

C.6. Why are you concerned about the patient's body temperature? What is normothermia for a burned patient?

Massively burned patients with loss of skin have constant evaporation from open surfaces. They tend to develop severe intraoperative hypothermia. The tendency is exaggerated by the effects of general anesthesia on the temperature-regulating centers, by vasodilation, and by the cool relatively dry environment of the operating room. The infusion of a large amount of intravenous fluids at room temperature also contributes to the development of hypothermia.

Normothermia for a burned patient is approximately 38.5° C because the burned patient develops a resetting of the centrally mediated thermostat.

Brunicardi FC, Anderson DK, eds. *Schwartz's Principles of Surgery*. 9th ed. New York: McGraw-Hill; 2010:197–205.

Herndon DN, ed. *Total Burn Care*. 3rd ed. Philadelphia: Saunders-Elsevier; 2007:205–206.

C.7. How is temperature best maintained?

Hypothermia is an ever-present problem. Burned patients have lost their natural insulation of the skin. Heat loss can occur through convection, conduction, and evaporation. Methods to maintain normothermia should involve active warming and prevention of heat loss. We administer all fluids and blood transfusions through the blood- and/or fluid-warming device. A thermal mattress or a bear-hugger is placed under a single-layer sterile sheet on the operating table and is prewarmed, although this method is not very effective. Warming the operating room to temperatures between 24° C (75.2° F) and 27° C (80.6° F) with a relative humidity higher than 50% is particularly effective. The areas of the patient's body not immediately involved in the surgery must be covered. Heated, humidified circuits are most effective in minimizing the heat loss from ventilation with cold anesthetic gases.

C.8. What derangements occur with hypothermia?

Hypothermia causes many physiologic changes. Hypothermia decreases metabolism, heart rate, CO, and blood pressure. At temperatures less than 28° C (82.4° F), atrial pacing becomes irregular and ventricular ectopic increases. Ventricular fibrillation occurs between 25° C (77° F) and 30° C (86° F) in the human adult.

Decreasing the rate of metabolism can prolong the duration of many anesthetic drugs. Decreased hepatic blood flow could slow the delivery of drugs to the site of metabolism.

Hypothermia shifts the oxygen dissociation curve to the left, resulting in a reduced release of oxygen by hemoglobin. However, the shift to the left is compensated by two factors, namely an increase in dissolved oxygen in the plasma and an increase in dissolved carbon dioxide, which increases acidity and tends to shift the curve to the right.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier/Churchill Livingstone; 2010:1542–1543.

C.9. What muscle relaxant would you use?

A nondepolarizing muscle relaxant should be used. Depolarizing relaxant should be avoided. In general, the choice of muscle relaxant should be based on the duration of the operation and the presence of any coexisting diseases that might affect the elimination of the drug. Muscle relaxants without histamine release would be preferred, such as vecuronium, and rocuronium.

C.10. Why is succinylcholine contraindicated in burned patients? For how long should it be avoided?

Succinylcholine is contraindicated in burned patients because injection of succinylcholine may cause a significant transient increase in serum potassium levels as high as 13 mEq per L, resulting in ventricular fibrillation and cardiac arrest. This hyperkalemic response begins approximately 5 to 15 days after the burn and persists for 2 to 3 months or longer, irrespective of degree and size of burn injury.

The exact mechanism responsible for this response is not known. Gronert and Theye postulated that the abrupt release of potassium is from the hypersensitive muscle membranes. Apparently, extrajunctional acetylcholine receptors are found on the muscle membranes of burned patients. Stimulation of these receptors may mediate the potentially lethal efflux of potassium.

The exact time for this hypersensitivity is unclear. Most authors recommend the avoidance of succinylcholine from 24 to 48 hours after the burn injury and extension of succinylcholine well until complete healing has occurred. A hyperkalemic response has been reported in a patient after 480 days. The recommended limit now is extended to approximately 2 years after the burned skin has healed.

Gronert GA, Theye RA. Pathophysiology of hyperkalemia induced by succinylcholine. *Anesthesiology*. 1975;43:89–99.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier/Churchill Livingstone; 2010:900.

Schaner PJ, Brown RL, Kirksey TD, et al. Succinylcholine-induced hyperkalemia in burned patients. *Anesth Analg*. 1969;48:764–770.

Tolmie JD, Joyce TH, Mitchell GD. Succinylcholine danger in the burned patient. *Anesthesiology*. 1967;28:467–470.

C.11. What other adverse effects are associated with succinylcholine?

Adverse effects of succinylcholine are many. Its side effects are as follows:

- Hyperkalemia, particularly following burns, spinal cord injuries, and generalized major trauma: a single case report of a marked hyperkalemic response to succinylcholine in a patient with a closed head injury without peripheral paralysis
- Increased intracranial and intraocular pressures: the practical importance of which is controversial
- Increased intragastric pressure: counterbalanced by the increase in lower esophageal pressure, which reduces or eliminates the increased risk of regurgitation
- Muscle pains: more likely to concern the patient with minor injuries who ambulates soon after surgery
- Prolonged paralysis in patients with atypical pseudocholinesterase
- Cardiac arrhythmias, particularly bradycardia after repeated doses
- Trigger for malignant hyperthermia

Miller RD, ed. *Miller's anesthesia*. 7th ed. Philadelphia: Elsevier/Churchill Livingstone; 2010:864–866.

C.12. How are the doses of nondepolarizing muscle relaxants affected by burn injury?

In general, burn patients show great resistance to the nondepolarizing relaxants. Martyn et al. first reported that burn patients required a five times higher plasma concentration of d-tubocurarine to attain a given percentage of twitch

depression compared with healthy subjects. The dose of pancuronium is increased by 2.5 times.

Although these patients have altered pharmacokinetics and increased plasma protein binding of the relaxants, most of the increased requirement appears to be due to alterations in the number and affinity of the junctional receptors. This alteration is quite variable.

Martyn JAJ, Liu LMP, Szyfelbein SK, et al. The neuromuscular effects of pancuronium in burned children. *Anesthesiology*. 1983;59:561–564.

Martyn JAJ, Szyfelbein SK, Ali HH, et al. Increased D-tubocurarine requirement following major thermal injury. *Anesthesiology*. 1980;52:352–355.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier/Churchill Livingstone; 2010:900.

C.13. How are the muscle relaxants such as succinylcholine, atracurium, cisatracurium, vecuronium, pancuronium, rocuronium, and curare metabolized and eliminated? Which of them has significant histamine release?

See Table 55.3.

C.14. What is the difference between metabolism and elimination of drugs?

Drug metabolism is the chemical modification of a substance. There are two phases: Phase I metabolism involves chemical reactions of oxidation, reduction, and hydrolysis. Many of these involve catalysis by the cytochrome P450 system in the liver. Phase II metabolism involves *conjugations*, or the combining of endogenous substances with drugs. This is also known as *the synthetic mode of biotransformation*.

Drug elimination involves all processes, which include metabolism, renal and hepatobiliary excretion, and pulmonary excretion such as CO_2 and anesthetic gases.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier/Churchill Livingstone; 2010:482.

Table 55.3 The Metabolism, Elimination, and Histamine Release of Muscle Relaxants

	ELIMINATION			
RELAXANT	KIDNEY (%)	LIVER (%)	PLASMA METABOLISM (%)	HISTAMINE RELEASE
Succinylcholine	<2	0	98	Slight
Atracurium	10–40	0	60–90	Slight
Cisatracurium	16	?	77	None
Vecuronium	40	60	0	None
Pancuronium	85	15	0	None
Rocuronium	25	70	0	None
d-turbocurarine	80	20	0	Moderate

Miller RD, ed. *Miller's Anesthesia*. 7th ed, Philadelphia: Elsevier/Churchill Livingstone; 2010:880,882.

D. Postoperative Management

D.1. How would you monitor this patient during transport?

This patient was most likely intubated, paralyzed, apneic, and still under the influence of general anesthetic. Monitoring should be directed toward respiration, oxygenation, and hemodynamics. These can be achieved by a transport monitor capable of monitoring ECG, blood pressure, CVP, and pulse oximeter. Ventilation should be controlled with an Ambu bag with supplemental oxygen during transport.

D.2. What is meant by diffusion hypoxia? How do you prevent it?

Fink et al. in 1954 first reported diffusion hypoxia during recovery from nitrous oxide–oxygen anesthesia. A mild degree of hypoxia may develop for more than 10 minutes when nitrous oxide–oxygen anesthesia is concluded and the patient is allowed to breathe room air. The arterial oxygen saturation may fall 5% to 10% and often reaches values less than 90% (Pao_2 <60 mm Hg). This occurs at the time when nitrous oxide is eliminated rapidly through the lungs. Nitrous oxide is 35 times more soluble in blood than nitrogen. Therefore, the amount of nitrous oxide diffused from blood to alveoli is much more than the amount of nitrogen diffused from alveoli to blood. Hence, alveolar oxygen is diluted by nitrous oxide. Diffusion hypoxia can be prevented by the inhalation of high concentrations of oxygen for several minutes before the patient is allowed to breathe room air.

Fink R. Diffusion anoxia. *Anesthesiology*. 1955;16:511–519.

Fink R, Carpenter SL, Holiday DA, et al. Diffusion anoxia during recovery from nitrous oxide-oxygen anesthesia. *Fed Proc*. 1954;13:354.

D.3. Why do patients often shiver in the recovery room on emergence from anesthesia?

Postanesthetic shivering is commonly observed in the recovery room. It is more commonly seen after receiving inhalational general anesthetics. It is thought that inhalation agents inhibit the temperature-regulating centers in the hypothalamus, and shivering is a thermoregulatory response to intraoperative hypothermia (the operating room is always cold). Shivering is a mechanism to produce heat to maintain normothermia. However, the precise mechanism of shivering is not fully explained because many patients who shiver are normothermic. It is postulated that the tremor pattern results from anesthetic-induced disinhibition of normal descending control over spinal reflexes. Similar nonthermoregulatory tremor has been seen in women during labor.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier/Churchill Livingstone; 2010:1543–1544.

D.4. Discuss the causes of oliguria in the recovery room.

Oliguria is defined arbitrarily as the production of less than 400 mL of urine in 24 hours. When oliguria occurs, it is a functional manifestation of various clinical entities referred to as *acute renal failure* (ARF). The syndrome of ARF may be classified into the following three groups:

- *Prerenal ARF (hypovolemic)*. There is no structural damage to the kidney. The reduction in renal blood flow results in a reduced filtration rate and a decrease in urinary

flow. It is reversible with volume expansion. However, if untreated, it can progress to the ischemic form of acute tubular necrosis.

- *Renal ARF (acute tubular necrosis)*. There is structural damage to the renal tubules. The damage may be due to ischemia or nephrotoxic substances.
- *Postrenal ARF (obstruction of urinary outflow)*. Pus, tubular debris, clots of blood, and crystalluria can cause bilateral obstruction of the ureters. The flow of urine is completely suppressed in contrast to the low flows found in prerenal and renal disease.

One must determine the cause of the oliguria because the management can vary greatly. To identify the cause of oliguria, one must make a careful assessment of the urinary sediment. Presence of renal tubular cells, renal tubular cell casts, and pigmented granular casts is strong evidence for the diagnosis of acute tubular necrosis. A normal urinary sediment supports a diagnosis of hypovolemic renal failure. Other data, such as CVP, PAOP, and pulmonary artery occlusion pressure can give valuable information about the state of hydration.

CHAPTER 56

Trauma

Danielle Lindenmuth, Jaideep K. Malhotra, and Ralph L. Slepian

A 31-YEAR-OLD MAN

sustained multiple stab wounds to the left upper quadrant of his abdomen and in the left hemithorax. Vital signs were as follows: blood pressure, 85/60 mm Hg; heart rate, 130 beats per minute; respiratory rate, 32 breaths per minute; temperature, 34.5° C (94.1° F). His hematocrit was 27%. He was emergently brought to the operating room for an exploratory laparotomy and possible thoracotomy.

A. Medical Disease and Differential Diagnosis

1. How is trauma classified?
2. What are the injuries associated with thoracic trauma?
3. What are the injuries associated with cardiac trauma?
4. What are the complications of acute pericardial tamponade?
5. What are the anesthetic implications for treating cardiac tamponade?
6. How is the initial assessment and management of the trauma patient performed?
7. What constitutes a primary survey and what is its objective?
8. What constitutes a secondary survey and what is its objective?
9. What are the signs and symptoms of a hemothorax? What is the definition of massive hemothorax?
10. What are the indications for a thoracotomy to treat a hemothorax?
11. How are pneumothoraces categorized?
12. What is an occult pneumothorax?
13. If the patient has a widened mediastinum on chest radiograph, what are your concerns?
14. What are the most commonly injured organs in blunt abdominal trauma?
15. What is a focused abdominal sonography for trauma (FAST) examination?
16. What is diagnostic peritoneal lavage?
17. Why was diagnostic peritoneal lavage not performed for this patient?

18. Define shock.
19. What are the four types of shock?
20. List the signs and symptoms of shock.
21. What is the pathophysiology of hypovolemic shock?
22. How would you classify hemorrhage?
23. What is the initial treatment of hemorrhagic shock?
24. Would you choose crystalloid or colloid therapy to treat hypovolemic shock?
25. Is there a place for dextran or hetastarch (Hespan) in treating hypovolemic shock?
26. Is there a place for hypertonic saline in the treatment of hypovolemic shock?

B. Preoperative Evaluation and Preparation

1. What premedication would you order?
2. What preoperative testing would you order?

C. Intraoperative Management

1. How would you monitor this patient?
2. How would you induce anesthesia?
3. What technique could you use if single-lung ventilation was indicated?
4. What agents would you choose to maintain anesthesia?
5. What muscle relaxant would you choose?
6. What can be done to decrease the incidence of intraoperative awareness?
7. Five minutes after intubation, the peak airway pressure increased from 20 to 40 cm H_2O. What are the possible causes?
8. How would you make a diagnosis of tension pneumothorax?
9. What is the treatment of tension pneumothorax?
10. The patient's blood loss was continuing and the hematocrit was 18%. What type of blood would you give if the type and crossmatch are not completed?
11. What precautions should be taken if more than 2 units of type O Rh-negative uncrossmatched whole blood is given?
12. What are the complications associated with any blood transfusion?
13. What is considered a massive transfusion?
14. What are the complications associated with a massive transfusion?
15. Can the shift of the oxygen–hemoglobin dissociation curve be quantitated?
16. How is hypothermia defined?
17. What are the adverse effects of hypothermia?
18. What is the treatment of hypothermia?
19. What are the effects of blood transfusion on the immune system?
20. What are the guidelines for transfusion of blood products?
21. What are the guidelines for the ratio of plasma/platelet transfusion to packed red blood cells in a massive transfusion?
22. If a patient were a member of the Jehovah's Witness religious sect, would you give a blood transfusion?
23. If a child is a Jehovah's Witness and suffered from hemorrhagic shock, what would you do?

D. Postoperative Management

1. What is acute respiratory distress syndrome (ARDS)? What is transfusion-related acute lung injury (ALI)?
2. How is ARDS treated?

3. In the recovery room, you are called to see this patient because of oliguria. How would you evaluate and treat this patient?
4. If this patient had a crush injury and low urine output, what other concerns might you have? What if the patient has dark or "tea-colored" urine?

A. Medical Disease and Differential Diagnosis

A.1. How is trauma classified?

Trauma is usually separated into two distinct categories: penetrating and blunt trauma. Both can cause havoc on the body's vascular, visceral, musculoskeletal, and nervous systems.

A.2. What are the injuries associated with thoracic trauma?

Penetrating injuries associated with thoracic trauma are typically associated with stabbings and gunshot wounds. The latter causes far more destruction because of the large amount of kinetic energy transferred to the thoracic cavity from the impact of the bullet. As a result, gunshot wounds to the thorax are diffuse and much more likely to be fatal compared to stabbings.

Blunt injuries to the chest are far more common than penetrating injuries. The most common causes of blunt injuries are deceleration injuries (as a result of motor vehicle accidents) and crush injuries. These can range from relatively minor injuries such as rib fractures to more severe ones such as lung contusion, tracheobronchial tears, flail chest, pneumothorax, hemothorax, injuries to the great vessels, and traumatic ruptures of the esophagus or diaphragm.

Kaplan JA, Slinger PD. *Thoracic Anesthesia*. 3rd ed. New York: Churchill Livingstone; 2003:315–326.

A.3. What are the injuries associated with cardiac trauma?

Penetrating cardiac injuries often lead to immediate cardiovascular collapse, and patients rarely survive to reach the operating room. Injuries associated with penetrating cardiac trauma include pericardial tamponade, cardiac perforation, rupture of a chamber, and fistula formation.

Blunt cardiac trauma injuries include cardiac contusion (most common), pericardial ruptures, rupture of a chamber, valvular tears, coronary artery injuries, and ventricular aneurysms.

Barash PG, Cullen BF, Stoelteg RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:904–905.

Kaplan JA, Slinger PD. *Thoracic Anesthesia*. 3rd ed. New York: Churchill Livingstone; 2003:315–326.

A.4. What are the complications of acute pericardial tamponade?

The primary complication of pericardial tamponade is a decrease in cardiac output secondary to pericardial pressure causing severe diastolic dysfunction. Unstable patients with acute pericadial tamponade present with hypotension, tachycardia, and tachypnea. The diagnosis can be made by the presence of Beck triad (hypotension, distended neck veins, and muffled heart sounds) and pulsus paradoxus, though these

signs can be easily missed on a hypovolemic trauma patient. Definitive diagnosis of cardiac tamponade can be made with transthoracic echocardiography. If the diagnosis of acute pericardial tamponade is made and the patient is unstable, immediate evacuation of the pericardium via a pericardiocentesis or a pericardial window is required. (Also see Chapter 11.)

Barash PG, Cullen BF, Stoelteg RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:904–905.

A.5. What are the anesthetic implications for treating cardiac tamponade?

The anesthetic goal for treating acute cardiac tamponade is to maintain intrinsic sympathetic tone. These patients are extremely dependent on intrinsic sympathetic tone, and therefore maintenance of heart rate and preload are of utmost importance. A preinduction intra-arterial catheter and large-bore intravenous access are essential. Ketamine and etomidate are considered appropriate agents for induction. A rapid-sequence induction with succinylcholine or an awake intubation can be performed. If possible, preinduction sedation should be avoided. Inotropes such as epinephrine should be readily available and can be given in small doses to avoid bradycardia and hypotension. Induction should be delayed until after patient preparation and draping is completed. In the event the patient becomes hemodynamically unstable, the effusion can then be drained as quickly as possible. (Also see Chapter 11.)

Barash PG, Cullen BF, Stoelteg RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:904–905.

A.6. How is the initial assessment and management of the trauma patient performed?

A systematic and organized approach to the assessment and management of the trauma patient has been developed by the American College of Surgeons and is taught as Advanced Trauma Life Support. Initial evaluation and management as stated by Advanced Trauma Life Support consists of five components:

1. The primary survey
2. Resuscitation
3. The secondary survey
4. Continued monitoring and reevaluation
5. Definitive care

Kaplan JA, Slinger PD. *Thoracic Anesthesia*. 3rd ed. New York: Churchill Livingstone; 2003:315–326.

A.7. What constitutes a primary survey and what is its objective?

The assessment of the trauma patient consists of the primary and secondary survey. The function of the primary survey is to identify and treat immediately life-threatening injuries. The life-threatening injuries associated with chest trauma are:

- Lost airway
- Tension pneumothorax
- Massive hemothorax
- Open pneumothorax

- Cardiac tamponade
- Flail chest

Kaplan JA, Slinger PD. *Thoracic Anesthesia*. 3rd ed. New York: Churchill Livingstone; 2003:315–326.

Thoracic trauma: Chest trauma initial evaluation. 2010. Available at: www.trauma.org/thoracic

A.8. What constitutes a secondary survey and what is its objective?

The secondary survey is a more detailed examination aimed at identifying other non–life-threatening injuries, planning further laboratory and radiographic studies, and forming a workable differential diagnosis. Examples of chest injuries identified on secondary survey are the following:

- Simple pneumothorax or hemothorax
- Rib fractures
- Pulmonary contusion
- Non–life-threatening blunt myocardial injury

Kaplan JA, Slinger PD. *Thoracic Anesthesia*. 3rd ed. New York: Churchill Livingstone; 2003:315–326.

Thoracic trauma: chest trauma initial evaluation. 2010. Available at: www.trauma.org/thoracic

A.9. What are the signs and symptoms of a hemothorax? What is the definition of massive hemothorax?

The signs and symptoms of a hemothorax include diminished breath sounds on the affected side, hemorrhagic shock, and mediastinal shift. A massive hemothorax is defined as a rapid accumulation of greater than 1,500 mL of blood in the thoracic cavity.

Reed AP, Yudkowitz FS. *Clinical Cases in Anesthesia*. 3rd ed. New York: Churchill Livingstone; 2005:481–493.

A.10. What are the indications for a thoracotomy to treat a hemothorax?

Hemothorax, if severe enough, can lead to hemorrhagic shock. Therefore, timely diagnosis and treatment are of utmost importance. After a chest tube is placed, if drainage of blood is greater than 1,200 mL or if drainage is greater than 200 mL per hour for over 4 hours, a thoracotomy is indicated. Alternatively, if the patient is older than 60 years, then if drainage is greater than 100 mL per hour for over 4 hours, a thoracotomy is also indicated. If the patient does not meet these criteria but is still hemodynamically unstable or if ventilation is difficult, emergent surgery should be performed.

Reed AP, Yudkowitz FS. *Clinical Cases in Anesthesia*. 3rd ed. New York: Churchill Livingstone; 2005:481–493.

A.11. How are pneumothoraces categorized?

Pneumothoraces are categorized into three broad categories: open, closed, and tension pneumothorax. Pneumothoraces, like hemothoraces, can cause severe hypoxemia, impair venous return, and cause a severe mediastinal shift.

Open pneumothoraces are a result of penetrating wounds and allow intrathoracic pressure to equalize with atmospheric pressure. The result is introduction of outside air every time the patient takes a breath. Definitive treatment is to close the wound and placement of a chest tube.

Closed pneumothoraces can result from both blunt and penetrating trauma to the chest. It is defined as the presence of air in the pleural space. Diagnosis can be made radiographically, via a chest radiograph or computed tomography (CT), though in many trauma situations, the patients' condition precludes obtaining a chest radiograph. In such cases, diagnosis can be made by physical examination, that is, by percussion or by diminished or absent breath sounds. In addition, a diagnosis can be made by ultrasound examination of the chest. Recent studies have suggested that using ultrasound detection of a pneumothorax can be a faster and more sensitive test than a supine chest radiograph. Treatment for a pneumothorax is the placement of a chest tube if the patient is unstable or if the pneumothorax is greater than 10% of the pleural cavity.

Tension pneumothorax is the progressive build-up of air within the pleural space that cannot escape. Essentially, it is a "one-way valve" that is exacerbated by positive pressure ventilation. This progressive build-up of air can cause a mediastinal shift, acute rise in airway pressures, and obstruction of venous return. All of these factors can result in a sudden and dramatic cardiovascular collapse.

Kaplan JA, Slinger PD. *Thoracic Anesthesia*. 3rd ed. New York: Churchill Livingstone; 2003:315–326.

Thoracic trauma: chest trauma—pneumothorax. 2010. Available at: www.trauma.org/thoracic

Wilkerson RG, Stone MB. Sensitivity to bedside ultrasound and supine anteroposterior chest for the identification of pneumothorax after blunt trauma. *Acad Emerg Med*. 2010;17:11–17.

A.12. What is an occult pneumothorax?

An occult pneumothorax is a pneumothorax that is diagnosed by CT but was not identified previously on the chest radiograph. In many cases, this type of pneumothorax is managed conservatively and resolves over time, without requiring placement of a chest tube. Frequently, a trauma patient with an occult pneumothorax will require general anesthesia and positive pressure ventilation. Whether these patients should have a chest tube placed pre-emptively is currently debated. For now, the decision should be made on a case-by-case basis.

When any trauma patient is placed on positive pressure ventilation, a history of a negative chest radiograph alone does not rule out the presence of an occult pneumothorax. As many as 50% of all pneumothoraces are occult, with an overall incidence of 5% in all trauma patients.

Ball CG, Kirkpatrick AW, Feliciano DV. The occult pneumothorax: what have we learned? *Can J Surg*. 2009;52:E173–E179.

Ouellet JF, Trottier V, Kmet L, et al. The OPTICC trial: a multi-institutional study of occult pneumothoraces in critical care. *Am J Surg*. 2009;197:581–586.

A.13. If the patient has a widened mediastinum on chest radiograph, what are your concerns?

A chest radiograph revealing a widened mediastinum may indicate the presence of a thoracic aortic injury. These types of injuries are often life threatening, necessitating

immediate identification and intervention. Blunt aortic injury is associated with high-speed deceleration and is the second leading cause of death in trauma patients, accounting for 16% of all trauma-related deaths. Open surgical repair requires a double lumen tube, single-lung ventilation, and clamping of the proximal aorta while taking measures to protect the spinal cord. In patients with coexisting injuries, such as increased intracranial pressure, profound bleeding, or hypoxemia, this procedure may be contraindicated. These patients may be medically managed with blood pressure control until these other issues have resolved. They may also be a candidate to undergo a less invasive endovascular repair, a technique that has been increasingly used over the last 20 years.

Ekah AP, Peterson W, Woods R, et al. Is chest x-ray an adequate screening tool for diagnosis of blunt thoracic aortic injury? *J Trauma*. 2008;65:1088–1092.

Neschis DG, Scalea TM, Flinn WR, et al. Blunt aortic injury. *N Engl J Med*. 2008;359:1708–1716.

A.14. What are the most commonly injured organs in blunt abdominal trauma?

In blunt abdominal trauma, the most commonly injured organs are the spleen, liver, kidneys, and bowel. Generally, blunt abdominal trauma leads to higher mortality rates than penetrating trauma. The reason is multifactorial and includes greater difficulty in diagnosis and frequent association with other injuries, such as head injury, chest trauma, and fractures.

A.15. What is a focused abdominal sonography for trauma (FAST) examination?

FAST is a rapid ultrasonography examination performed in the trauma resuscitation room. It has been used to determine the presence of fluid (blood) within the peritoneum, pericardium, and thorax. Currently, FAST is particularly helpful in the bedside examination of hemodynamically unstable blunt trauma patients. It may also have a role in some patients with penetrating trauma.

Rozycki GS, Root DH. The diagnosis of intraabdominal visceral injury. *J Trauma*. 2010:1019–1022.

Trauma ultrasonography—the FAST and beyond. 2007. Available at: www.trauma.org/radiology/FASTintro.html

A.16. What is diagnostic peritoneal lavage?

In penetrating trauma, diagnostic peritoneal lavage allows for rapid identification of a hemoperitoneum and therefore the discovery of an intraperitoneal injury. Peritoneal lavage is a procedure performed in the emergency room to help determine whether a patient has internal bleeding that requires an exploratory laparotomy. It is done by performing a mini-laparotomy under local anesthesia. A catheter is then placed into the abdomen and is aspirated for gross blood. Aspiration of 10 mL of blood is considered a positive finding. A grossly bloody aspirate is indicative of solid or vascular injury. If less than 10 mL of blood is aspirated, then 1 L of lactated Ringer's solution or normal saline is allowed to drain into the abdomen. The lavage fluid is then allowed to return by gravity and is sent to the laboratory for analysis. Criteria for a positive peritoneal lavage are an erythrocyte count of 100,000 per mm^3, a white blood cell count of 500 per mm^3, the presence of bile or food particles, and

a fluid amylase concentration of 175 units per dL. The white blood cell level itself should not determine the need for laparotomy. The level of white blood cells also does not rise initially, but requires several hours to rise. Alkaline phosphatase and amylase are contained in the small bowel and spill into the abdominal cavity after injury. These levels tend to rise early in injury. Amylase in lavage fluid has been seen as a more accurate marker than alkaline phosphatase. If the peritoneal lavage meets one or more of these criteria, the patient comes to the operating room for an exploratory laparotomy.

Runyan MS, Marx JA. Peritoneal procedures. In: Roberts JR, Hedges JR, eds. *Clinical Procedures in Emergency Medicine*. 5th ed. Philadelphia: WB Saunders; 2009:773–789.

A.17. Why was diagnostic peritoneal lavage not performed for this patient?

Peritoneal lavage was not done for two reasons. First, it is felt that all penetrating wounds to the abdomen need to be surgically explored. Second, this patient was exhibiting signs of shock and obviously needed to be sent to the operating room without delay.

Before CT and ultrasonography technologies, diagnostic peritoneal lavage was the only diagnostic test available to rapidly evaluate the abdomen for injury. Although diagnostic peritoneal lavage is highly sensitive, it can also result in false positive results, leading to unnecessary exploratory laparotomies. CT now allows for evaluation of all intraperitoneal organs, the diaphragm, and the retroperitoneum (an area inaccessible to diagnostic peritoneal lavage), while also allowing for identification of the specific organ injured. CT should be used in the evaluation of hemodynamically stable trauma patients.

Rozycki GS, Root DH. The diagnosis of intraabdominal visceral injury. *J Trauma*. 2010;68:1019–1022.

A.18. Define shock.

Shock is defined as the circumstance of insufficient oxygen delivery to sustain aerobic metabolism in vital cells of essential organs. Shock of all forms appears to be invariably related to inadequate tissue perfusion. The low-flow state in vital organs seems to be the final common denominator in all forms of shock.

Mullins R. Shock, electrolytes and fluid. In: Townsend CM, ed. *Sabiston Textbook of Surgery*. 18th ed. Philadelphia: WB Saunders; 2007:69–112. Available at: MD Consult online database: http://www.mdconsult.com.

A.19. What are the four types of shock?

For a working classification of shock, the following classification offered by Blalock in 1934 is still useful and functional:

- *Hematogenic (hypovolemic, hemorrhagic) shock:* Characterized by a loss of circulatory blood volume.
- *Cardiogenic shock:* Characterized by an inability of the myocardium to pump blood.
- *Vasogenic (septic) shock:* Characterized by an infection that causes a decrease in peripheral vascular resistance.
- *Neurogenic shock:* Characterized by an impairment of the central nervous system–mediated control of vascular tone.

Mullins R. Shock, electrolytes and fluid. In: Townsend CM, ed. *Sabiston Textbook of Surgery*. 18th ed. Philadelphia: WB Saunders; 2007:69–112. Available at: MD Consult online database: http://www.mdconsult.com.

A.20. List the signs and symptoms of shock.

Tachycardia, hypotension, cool extremities, pallor, oliguria, tachypnea, decreased capillary refill, anxiety, restlessness, and loss of consciousness are signs and symptoms of shock.

A.21. What is the pathophysiology of hypovolemic shock?

Cardiovascular derangement

An acute decrease in circulating blood volume leads to an increase in sympathetic activity with an outpouring of epinephrine and norepinephrine from the adrenal gland. The α-adrenergic response causes vasoconstriction, which shunts blood from the skin, viscera, and muscle, thereby preserving the coronary and cerebral circulation. With constriction of both precapillary and postcapillary sphincters, a reduction occurs in hydrostatic pressure of the capillary bed, which allows the osmotic pressure to draw fluid back into the vascular space from the interstitial space. This process of hemodilution tends to expand the patient's blood volume. In addition to the vasoconstriction and hemodilution, a tachycardic response may be noted.

Myocardial-depressant factor is a peptide thought to be released from the pancreas during low-flow states. This peptide is thought to be responsible for some of the decreased cardiac performance seen in trauma patients. Pancreatectomy and various myocardial-depressant factor antagonists demonstrate protective myocardial effects during shock in animals.

Acid–base disturbance

Metabolic acidosis is almost always seen in association with a shock state. As a result of decreased blood flow or a low rate of perfusion, oxygen delivery to vital organs is reduced and consequently a mandatory change occurs from aerobic to anaerobic metabolism. This shift will lead to the production of lactic acid instead of carbon dioxide as the end product of metabolism. The increase in lactic acid leads to a metabolic acidosis.

Jones EA, Kline JA. Shock. In: Marx JA, Hockberger RS, Walls RM, et al., eds. *Rosen's Emergency Medicine: Concepts and Clinical Practice*. 7th ed. St. Louis: Mosby; 2009:34–41.

Mullins R. Shock, electrolytes and fluid. In: Townsend CM, ed. *Sabiston Textbook of Surgery*. 18th ed. Philadelphia: WB Saunders; 2007:69–112. Available at: MD Consult online database: http://www.mdconsult.com.

A.22. How would you classify hemorrhage?

Classification of hemorrhage based on blood loss is as follows:

Class I: Blood loss of up to 15% of the blood volume: normal pulse and blood pressure
Class II: Blood loss of up to 30% of the blood volume: tachycardia, decreased urine output, and anxiety
Class III: Blood loss of up to 40% of the blood volume: marked tachycardia, hypotension, tachypnea, oliguria, and anxiety
Class IV: Blood loss of more than 40% of the blood volume: tachycardia and hypotension, tachypnea, anuria, confusion, and lethargy

Dutton RP. Shock and trauma anesthesia. *Anesthesiol Clin North Am*. 1999;17:83–95.

A.23. What is the initial treatment of hemorrhagic shock?

The initial treatment of hemorrhagic shock is to attempt to stabilize hemodynamics by administering fluids and blood products as required to maintain tissue perfusion and oxygen delivery. Recently, trauma centers have revised the standard approach to resuscitation for major traumatic hemorrhage requiring massive transfusion. Trauma centers have adapted the practice of initial resuscitation with hemostatic components such as plasma and platelets, as well as packed red blood cells. This strategy for treating massive hemorrhage was pioneered from knowledge gained from combat hospitals in Iraq and Afghanistan. This approach involves limiting the total volume of crystalloid and replacing intravascular volume with packed red blood cells and fresh frozen plasma (FFP) in a ratio approaching 1:1. This strategy is geared to avoid the acute coagulopathy associated with major trauma and blood loss and has been shown to decrease mortality rates in combat and civilian injuries requiring massive transfusion.

Barash PG, Cullen BF, Stoelteg RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:904–905.

Griffee MJ, Deloughery TG, Thorborg PA. Coagulation management in massive bleeding. *Curr Opin Anaesthesiol*. 2010;23:263–268.

A.24. Would you choose crystalloid or colloid therapy to treat hypovolemic shock?

Crystalloid solutions can sustain hemodynamics and deliver adequate oxygenation in healthy patients who have lost as much as 30% of their total blood volume. Still, controversy remains over the use of crystalloid versus colloid therapy for the initial therapy of hypovolemic shock.

Proponents of crystalloid therapy believe that both intravascular and interstitial fluid losses occur in hypovolemic shock and that these can be readily replaced with crystalloids. Another benefit of crystalloids is the decrease in blood viscosity, which may enhance perfusion. A particular advantage to lactated Ringer's solution is that lactate is metabolized to bicarbonate, which may help to buffer the patient's acidosis. Finally, in this age of medical economics, the cost of crystalloid is much less than that of colloid. Because crystalloid leaves the intravascular space and enters the interstitial space, large quantities are needed, and some fear that these quantities may lead to both pulmonary and peripheral edema, although studies have not confirmed this fear.

Proponents of colloid therapy, on the other hand, argue that much less volume of fluid is needed to counteract hypovolemic shock and that early colloid therapy can prevent the complications associated with large-volume crystalloid resuscitation such as dilutional coagulopathy, hyperchloremic acidosis, and edema. Colloids maintain the oncotic pressure and hold the interstitial fluids in the intravascular space, which is felt to possibly prevent pulmonary edema. If leaky alveolar capillary membranes are seen within the lung, colloids may worsen pulmonary edema.

Choi P, Yip G, Quinonez L, et al. Crystalloids vs. colloids in fluid resuscitation: a systematic review. *Crit Care Med*. 1999;27:200–209.

Kaye AD, Riopelle JM. Intravascular fluid and electrolyte physiology. In: Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:1705–1738.

Orlinsky M, Shoemaker W, Reis E, et al. Current controversies in shock and resuscitation. *Surg Clin North Am*. 2001;81:1217–1262.

A.25. Is there a place for dextran or hetastarch (Hespan) in treating hypovolemic shock?

Dextran and hetastarch are synthetic polysaccharide solutions with varying mean molecular weights. Dextran 40, dextran 70, and hetastarch have all been used as volume expanders. Dextrans are relatively inexpensive, increase effective blood volume, and decrease blood viscosity. Nevertheless, their negative aspects are considerable. They impair coagulation by coating platelets, and they impair typing and crossmatching by coating red blood cells. In addition, anaphylactic reactions have been reported.

A.26. Is there a place for hypertonic saline in the treatment of hypovolemic shock?

Hypertonic saline is now being used for resuscitation at some major centers. Its effects tend to be of short duration, so it is not used alone. It is under investigation as a resuscitative agent, particularly in the prehospital setting, because small volumes may have beneficial cardiovascular effects. If one combines hypertonic saline and dextran, the effective resuscitation will be prolonged. Hypertonic saline is usually supplied as 7.5% NaCl, often combined with a colloid, 6% dextran 70. The optimal dose is thought to be 4 mL per kg.

The potential advantage is that the greater the sodium concentration, the less total volume will be required for resuscitation. A serious potential danger exists in that patients may become hypernatremic, which can lead to brain dehydration. In patients with high intracranial pressure, this brain dehydration may have a potential benefit in lowering it.

Hypertonic saline solutions have been used successfully in hemorrhagic shock resuscitation in animals and humans. This type of fluid resuscitation offers the advantage of requiring smaller volumes for a similar effect (4 to 5 mL per kg), making it especially attractive for use during prehospital resuscitation. Hypertonic saline has been shown to elevate mean arterial pressure and cardiac output and increase renal, mesenteric, total splanchnic, and coronary blood flow. It causes a small and transient rise in circulating volume by transcapillary refill. These beneficial effects after controlled hemorrhage have been established. Its hypertonic nature and small volume usage are particular advantages in traumatic brain injury. Hypertonic saline promotes redistribution of fluid into the vascular compartment and decreases intracranial pressure. It also seems to offer similar advantages to improvement in microcirculatory flow of the spinal cord. Use of these products during uncontrolled hemorrhage, nevertheless, has been strongly questioned.

Henry S, Scalea T. Resuscitation in the new millennium. *Surg Clin North Am.* 1999;79:1259–1267.

Jones EA, Kline JA. Shock. In: Marx JA, ed. *Rosen's Emergency Medicine: Concepts and Clinical Practice*. 7th ed. St. Louis: Mosby; 2009:34–41.

McCunn M, Karlin A. Nonblood fluid resuscitation: more questions than answers. *Anesthesiol Clin North Am.* 1999;17:107–123.

Orlinsky M, Shoemaker W, Reis E, et al. Current controversies in shock and resuscitation. *Surg Clin North Am.* 2001;81:1217–1262.

B. Preoperative Evaluation and Preparation

B.1. What premedication would you order?

None. This is a critically ill patient who is coming to the operating room for emergency surgery. Narcotics and sedatives would be contraindicated because they could worsen his already tenuous hemodynamic state.

B.2. What preoperative testing would you order?

Because of the emergent nature of the trauma setting, preoperative tests and imaging studies are frequently limited. If the patient is hemodynamically unstable, any preoperative evaluation is aborted and the patient is taken directly to the operating room.

If the patient is stable, a portable chest radiograph, arterial blood gas, complete blood count, and FAST can be obtained in a relatively short period in the emergency department or operating room before surgery. Often, these tests can be obtained while the patient is being prepared for emergency surgery. This information can be combined with other monitoring adjuncts such as oxygen saturation, invasive blood pressure, and electrocardiogram to evaluate the patient and formulate an appropriate management strategy. Although it is usually not possible to clinically clear the c-spine before surgery, it is important to know the results of any radiologic studies that have been done, in order to rule out an unstable cervical spine fracture, or adjust anesthetic plan accordingly.

C. Intraoperative Management

C.1. How would you monitor this patient?

Routine noninvasive monitor would include electrocardiogram, blood pressure cuff, oxygen monitor, pulse oximeter, end-tidal carbon dioxide, esophageal stethoscope, temperature probe, and Foley catheter.

Invasive monitors for this patient would include an arterial line and a central venous catheter. An arterial line is useful for blood sampling and direct blood pressure monitoring. The central venous line is helpful for determining the patient's volume status. A pulmonary artery catheter may be indicated if the patient shows signs of heart failure.

C.2. How would you induce anesthesia?

Because all trauma patients are considered to have a full stomach, the best way to protect the patient's airway is to perform a rapid-sequence induction with cricoid pressure while maintaining in-line cervical immobilization of the c-spine for any patient in a c-collar. For the patient with a suspected difficult airway, one could do an awake fiberoptic intubation. Awake fiberoptic intubation in this population can be difficult, because they may be confused, uncooperative, and sometimes even combative. First, if tolerated, the patient should be preoxygenated for 3 to 5 minutes. Next, ketamine 1 to 2.5 mg per kg, might be given followed by succinylcholine 1.5 mg per kg while maintaining cricoid pressure. Ketamine was chosen in this case because of its cardiovascular-stimulating effects and the patient's unstable hemodynamics. Etomidate (0.2 mg per kg) would be another appropriate choice for an induction agent. If the patient was adequately resuscitated in the emergency room and is hemodynamically stable, one could possibly use a small dose of thiopental or midazolam or fentanyl for induction.

If the patient is comatose, in severe shock, or in full arrest on admission to the resuscitation room, no drug other than oxygen and possibly a neuromuscular blocking drug is required until the patient's blood pressure and heart rate sufficiently rebound so anesthetics can be titrated. In awake traumatized patients who are thought to be hypovolemic, etomidate is best tolerated.

Wilson WC, Patel N, Hoyt DB, et al. Perioperative anesthetic management of patients with abdominal trauma. *Anesthesiol Clin North Am.* 1999;17:211–236.

C.3. What technique could you use if single-lung ventilation was indicated?

If the patient does not already have a secure airway, the airway should be secured in the manner described in the previous question. Single-lung ventilation is indicated in this situation if the patient is bleeding from one lung and protection of the other lung is required or to improve the surgical field (lower priority). Once the airway is secured, there are several ways to obtain single-lung ventilation. The easiest and safest technique would be to use an Arndt or Cohen bronchial blocker thorough the endotracheal tube. If those blockers are not available, one could pass an embolectomy catheter (bronchial blocker) in the trachea and then the endotracheal tube. The bronchial blocker could then be positioned under direct vision using fiberoptic bronchoscopy. Alternatively, the bronchial blocker could be placed through a bronchoscopy adapter and endotracheal tube, and its position can be confirmed by fiberoptic bronchoscopy. The point at which the bronchial blocker enters the bronchoscopy adapter can then be sealed with pliable "bone wax" (a form of sterile bees wax that is soft and kneadable).

Another method of obtaining single-lung ventilation would be to change the endotracheal tube to a double-lumen tube through a Cook exchange catheter. The major risks of this option are losing a previously secured airway and aspiration while attempting to change the tube.

C.4. What agents would you choose to maintain anesthesia?

As the patient stabilizes and the hemodynamics improve, other anesthetic agents can be carefully titrated to prevent hypotension, as follows:

- Sedatives or amnestics should be added to the anesthetic as soon as tolerated. Remember to start with small doses and check the patient's reaction to the drugs between doses.
- Opioids should be titrated to control the hemodynamic response to surgery.
- Nitrous oxide must be carefully considered, because it has the capacity to accumulate in closed airspaces or because of the high possibility that this patient has an occult pneumothorax.
- Inhalational anesthetics may be used in low concentrations so the patient's hemodynamics are not compromised.

C.5. What muscle relaxant would you choose?

Vecuronium, rocuronium, and cis-atracurium are free of cardiovascular side effects and have an intermediate duration of action. They are acceptable choices. Pancuronium is a long-acting muscle relaxant with vagolytic properties that may be deleterious to the patient.

Curare, metocurine, atracurium, and mivacurium all have the potential to cause hypotension and therefore would not be chosen for this patient.

C.6. What can be done to decrease the incidence of intraoperative awareness?

The incidence of intraoperative awareness is commonly cited as approximately 0.2%. This is probably an overestimation. In other sources, the incidence of traumatic intraoperative recall associated with pain is less that 0.03%. The American Society of Anesthesiologists Closed Claims database states that claims associated to recall during anesthesia constitute 1.5%. An increased relative risk for recall is seen in certain types of surgery, including cardiac surgery, cesarean sections, and trauma surgery. This most likely represents intentional light anesthesia associated with higher levels of stimulation. Recently, the Bispectral Index by Aspect Medical Systems (Natick, MA) and the PSA 4000 by Physiometrix (Billerica, MA) have been used as monitors of intraoperative awareness. It has been shown that patients with a Bispectral Index value of 50 were able to respond to verbal commands less than 10% of the time. Although

this information may be potentially useful, the application of these monitors during a trauma resuscitation may not be easily accomplished.

Kerssens C, Klein J, vander Woerd A, et al. Auditory information processing during adequate propofol anesthesia monitored by electroencephalogram Bispectral Index. *Anesth Analg*. 2001;92:1210–1214.

Lubke GH, Kerssens C, Gershon RY, et al. Memory function droning general anesthesia for emergency cesarean sections. *Anesthesiology*. 2001;92:1029–1034.

O'Connor MF, Daves SM, Tung A, et al. BIS monitoring to prevent awareness during general anesthesia. *Anesthesiology*. 2001;94:520–522.

Rampil I. Monitoring depth of anesthesia. *Curr Opin Anesthesiol*. 2001;14:649–653.

C.7. Five minutes after intubation, the peak airway pressure increased from 20 to 40 cm H_2O. What are the possible causes?

The possible causes of peak airway pressure increase are as follows:

- Tension pneumothorax
- Bronchospasm
- Endobronchial intubation
- Pulmonary edema
- Secretions
- Kink in the anesthesia circuit or endotracheal tube

C.8. How would you make a diagnosis of tension pneumothorax?

A tension pneumothorax can be diagnosed by the absence of breath sounds on the affected side. The chest movement may be asymmetric. Neck veins will be full, and systemic hypotension can occur if the tension pneumothorax is severe. Any patient who deteriorates under anesthesia and has wounds to the upper abdomen, lower neck, or ribs should be assumed to have a tension pneumothorax until proven otherwise.

Eckstein M, Henderson SO. Thoracic trauma. In: Marx JA, Hockberger RS, Walls RM, et al., eds. *Rosen's Emergency Medicine: Concepts and Clinical Practice*. 7th ed. St. Louis: Mosby; 2009:387–397.

C.9. What is the treatment of tension pneumothorax?

Immediate decompression of the chest is mandatory for tension pneumothorax because a patient's hemodynamics will deteriorate. Diagnosis is made clinically and not by a chest radiograph. An 16 or 18-gauge Angiocath is placed into the second intercostal space at the midclavicular plane. After the air escapes, confirming your diagnosis, and the lung is decompressed, a chest tube should be placed.

Eckstein M, Henderson SO. Thoracic trauma. In: Marx JA, Hockberger RS, Walls RM, et al., eds. *Rosen's Emergency Medicine: Concepts and Clinical Practice*. 7th ed. St. Louis: Mosby; 2009:387–397.

C.10. The patient's blood loss was continuing and the hematocrit was 18%. What type of blood would you give if the type and crossmatch are not completed?

This patient should have blood transfused as soon as possible. Type O Rh-negative packed cells are the universal donor. This should be started while type-specific blood

is being made available. Whenever the type-specific blood is ready, one can switch to it. If the transfusion begins with type O Rh-negative *whole blood* and more than 2 units has been infused, only type O Rh-negative blood should continue to be used. Usually, by the time a patient reaches the operating room from the emergency room, a partial crossmatch can be done. This usually takes 5 to 10 minutes, after which time type-specific blood can be transfused.

Gorgas D. Transfusion therapy. In: Roberts JR, ed. *Clinical Procedures in Emergency Medicine*. 5th ed. Philadelphia: WB Saunders; 2009: 483–80.

Miller R. Transfusion therapy. In: Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010: 1739–1766.

C.11. What precautions should be taken if more than 2 units of type O Rh-negative uncrossmatched whole blood is given?

The plasma from type O Rh-negative *whole blood* contains anti-A and anti-B antibodies, which can cause hemolytic reactions with type A and type B blood cells if given in significant quantities. Therefore, only type O Rh-negative blood should continue to be transfused, although this will lead to minor hemolysis of the patient's own red blood cells. The patient should not receive his type-specific blood until the blood bank determines that the transfused anti-A and anti-B antibody levels have fallen sufficiently low to permit safe transfusion of type-specific blood. This usually requires a 2-week waiting period.

Packed red blood cells have smaller volumes of plasma and are virtually free of anti-A and anti-B antibodies. Therefore, whenever type-specific blood is not yet available, type O Rh-negative uncrossmatched packed red blood cells should be used in preference to type O Rh-negative *whole blood*. Once type-specific blood is available, it can be used safely.

Cain JG. Current practices in fluid and blood component therapy in trauma. *Semin Anesth*. 2001;20:28–35.

Miller R. Transfusion therapy. In: Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:1739–1766.

C.12. What are the complications associated with any blood transfusion?

Complications associated with blood transfusion are as follows:

Transfusion reactions

- Febrile reactions occur in approximately 1% of all transfusions. In an awake patient, this is usually no more than an annoyance that requires decreasing the infusion rate.
- Allergic reactions to properly crossmatched blood will manifest as an increase in temperature, pruritus, and urticaria. This may be difficult to diagnose in the anesthetized patient. Treatment consists of administration of antihistamines and discontinuation of the transfusion.
- Hemolytic reactions occur when incompatible blood is administered. Caused by activation of the complement system, they can be life threatening. In the awake patient, fever, chills, dyspnea, substernal, and lumbar pain are seen in addition to hypotension. Under general anesthesia, the only sign that is not masked is hypotension. Also, if free hemoglobin can be documented in the plasma or urine, this too would be indicative of a transfusion reaction. Substances released by the hemolyzed cells can lead to disseminated intravascular

coagulation (DIC) and acute renal failure (ARF). Treatment consists of immediate discontinuation of the transfusion. Hypotension should be treated with hydration, vasopressors, and inotropic agents if needed. Urinary output must be maintained by adequate hydration. Although its value is uncertain, sodium bicarbonate has been used to alkalinize the urine to improve the solubility of the hemoglobin-degradation products. The risk of an ABO-incompatible transfusion is 1:33,500 red blood cell transfusions. Mortality associated with this remains high, at approximately 40%.

Transmission of disease

- Transmission of disease can be a serious problem. HIV, hepatitis B virus, hepatitis C virus, and cytomegalovirus can all be transmitted by transfusion. Because the risk of disease transmission increases with each unit of blood or its components given, they must be carefully scrutinized before they are administered. Currently, the incidence of posttransfusion HIV infection is 1:1,780,000 per transfused unit of blood. The risk of hepatitis B transmission is approximately 1 per 269,000 units. The risk of hepatitis C transmission is 1:1,600,000 per unit transfused. Cytomegalovirus is the most common viral agent transmitted by blood transfusion; it produces clinically important infections only in immunodepressed patients. Malaria, syphilis, Lyme disease, Chagas disease, and other diseases may also be transmitted through transfusion of blood and blood products. The aggregate infection risk is approximately 1 per 34,000. As new nonhemoglobin solutions appear on the market, less blood will be transfused and disease transmission will diminish.

Microembolization

- Microembolization can occur from the transfusion of blood or its components. Stored blood forms microaggregates that are too small to be removed by the standard 170-micron blood filters. Smaller filters have been developed to remove these particles. When using blood filters of the 20- to 40-micron range, the rate of transfusion is dramatically decreased because of the increased resistance of the filters. Some early reports suggested that these microaggregates may lead to pulmonary dysfunction, but this has never been proven.

Drummond JC , Petrovitch CT, Lane TA. Hemostasis and transfusion medicine. In: Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:370–377.

Galel S, Nguyen D, Fontaine M, et al. Transfusion medicine. In: Greer JP, Wintrobe MM, eds. *Wintrobe's Clinical Hematology*. 12th ed. Philadelphia: Lippincott Williams & Wilkins; 2008:672–721.

Goodnough LT. Transfusion medicine. In: Goldman L, Schafer AI eds. *Goldman: Goldman's Cecil Medicine*. 24th ed. Philadelphia: Saunders; 2011: Available at: MD Consult online database: www.mdconsult.com. Print edition not yet available.

Kruskall MS, Mintz PD, Bergin JJ, et al. Transfusion therapy in emergency room medicine. *Ann Emerg Med*. 1988;17:329–331.

Landers DF, Dullye KK. Vascular access and fluid resuscitation in trauma: issues of blood and blood products. *Anesthesiol Clin North Am*. 1999;17:125–135.

Miller RD, ed. Transfusion therapy. In: *Miller's Anesthesia*. 7th ed. New York: Churchill Livingstone; 2010:1739–1766.

Schreiber GB, Busch MP, Kleinman SH, et al. The risk of transfusion-transmitted viral infections. *N Engl J Med*. 1996;334:1685–1690.

Spahn DR, Casutt M. Eliminating blood transfusions: new aspects and perspectives. *Anesthesiology*. 2000;83:242–255.

C.13. What is considered a massive transfusion?

A massive transfusion is defined as the replacement of the patient's total blood volume in a 24-hour period. This is usually between 8 and 10 units of packed red blood cells. Many trauma cases far exceed this amount and may require other blood components in addition to the red blood cells.

Miller RD, ed. Transfusion therapy. In: *Miller's Anesthesia*. 7th ed. New York: Churchill Livingstone; 2010:1739–1766.

C.14. What are the complications associated with a massive transfusion?

Complications of a massive transfusion include hypothermia, acidosis, coagulopathy, DIC, fibrinolysis, citrate toxicity, hyperkalemia, hypokalemia, acid–base imbalance, and impaired hemoglobin function.

- Hypothermia is an obvious consequence of infusing cold banked blood. Therefore, it is recommended that the blood be reconstituted with warm normal saline. In addition, all fluids should pass through a warming device and the operating room should be kept warm, in order to help prevent hypothermia .
- The coagulopathy associated with trauma is multifactorial. It is a combination of thrombocytopenia and dilutional and consumptive factors. Furthermore, the systemic inflammatory response syndrome that is associated with trauma produces activated protein C, an anticoagulant. In addition, hypothermia and acidosis are commonly seen during massive transfusions and this worsens the coagulopathy. Both platelets and coagulation factors are markedly decreased and must be replaced. They should be administered after laboratory documentation of the deficiency. It is no longer accepted practice to give FFP routinely after 5 units of packed red blood cells, and it is not proper to give platelets after 10 units of packed red blood cells. DIC and fibrinolysis may occur after massive transfusions. An important triggering event of DIC and fibrinolysis is shock, with its accompanying tissue ischemia, acidemia, and waste product accumulation. Therefore, early and prompt treatment of hypoperfusion is mandatory.
- Citrate toxicity is frequently discussed, but it is rarely a problem. However, in the pediatric population, citrate toxicity is much more of a problem and should be considered in any child who does not respond to rapid volume administration of blood products. Citrate is added to stored blood to bind calcium and therefore prevent clotting. Citrate binds calcium and decreases the patient's ionized calcium level. Hypocalcemia may present as a prolongation of the QT interval with little effect of cardiac performance. In some cases, ventricular performance may be compromised. Cardiac performance also may be decreased by acidemia, hyperkalemia, and hypothermia, which all accompany the shock state. Citrate is metabolized to bicarbonate, and it can contribute to posttransfusion metabolic alkalosis.
- Hyperkalemia can be a rare occurrence in the massively transfused patient. Plasma potassium levels of stored whole blood range between 12 and 32 mEq per L. The potassium level increases approximately 1 mEq/L/day in stored blood. A unit of whole blood would contain between 4 and 8 mEq of potassium, which is hardly enough to cause hyperkalemia. A unit of packed red blood cells contains insignificant amounts of potassium because most plasma is removed. However, in the shock state with hypoperfusion and acidemia, hyperkalemia may become evident.
- Hypokalemia is also a possibility after a massive transfusion. Citrate is metabolized to bicarbonate, resulting in a metabolic alkalosis that can cause hypokalemia. In addition, the transfused red blood cells take up potassium, which can also result in hypokalemia.
- Acid–base imbalance is a problem after massive transfusion. Banked blood with a pH level of 6.8 is acidotic and may worsen the acidosis that accompanies shock.

This acidosis is easily reversible with the restoration of normal perfusion. No need is seen to give supplemental bicarbonate based on an arbitrary number of units transfused. Nevertheless, if metabolic acidosis persists, sodium bicarbonate is warranted. As stated, citrate from stored blood and lactate from lactated Ringer's solution are metabolized to bicarbonate, and this can cause metabolic alkalosis.

- Impaired hemoglobin function is a theoretic possibility after massive transfusion. The 2,3-diphosphoglycerate level is decreased in banked blood. This will shift the oxygen–hemoglobin dissociation curve to the left, and oxygen will be held more tightly by the hemoglobin molecule. No studies have documented any adverse effects from this.

Drummond JC, Petrovitch CT. The massively bleeding patient. *Anesthesiol Clin North Am*. 2001;19:633–649.

Goskowicz R. The complications of massive blood transfusion. *Anesthesiol Clin North Am*. 1999;17:959–978.

Miller RD, ed. Transfusion medicine. In: *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:1739–1766.

C.15. Can the shift of the oxygen–hemoglobin dissociation curve be quantitated?

Yes, the shift of the oxygen–hemoglobin dissociation curve is quantified by means of the P_{50} values (i.e., the partial pressure of oxygen at which hemoglobin is 50% saturated with oxygen). A leftward shift of the curve indicates a low P_{50} value. The normal P_{50} value of blood is 27 mm Hg and the normal level of 2,3-diphosphoglycerate is 4.8 mmol per mL of erythrocytes.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 6th ed. Philadelphia: Butterworth-Heinemann; 2009:463–475.

C.16. How is hypothermia defined?

Hypothermia is defined as a core body temperature of less than 35° C (95° F). A trauma patient brought to the emergency room may already be hypothermic. Prolonged exposure to a cold operating room, evaporative heat loss from the respiratory tract, infusions of cold fluids, and loss of heat production secondary to shock cause decreased core temperature in most patients.

All skin surfaces not in the surgical field should be covered to reduce convective and radiant heat loss. Humidification of inspired gases reduces evaporative heat loss from the lung. All intravenous fluids should be warmed.

Warming the operating room may also lessen heat loss, as will the use of warming blankets.

Gorgas DL. Transfusion therapy. In: Roberts JR, ed. *Clinical Procedures in Emergency Medicine*. 4th ed. Philadelphia: WB Saunders; 2009:463–475.

Sessler D. Temperature regulation and monitoring. In: Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:1533–1556.

C.17. What are the adverse effects of hypothermia?

- Shivering-induced increase in oxygen consumption by as much as 400%
- A leftward shift in the oxygen–hemoglobin dissociation curve

- Decreased coagulation of blood (10% reduction in coagulation factor activity for every 1° C drop in body temperature)
- Increased epinephrine and norepinephrine levels, causing vasoconstriction
- As hypothermia becomes severe, possible decreases in both heart rate and blood pressure
- Cardiac arrhythmias that can progress to ventricular fibrillation

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2005: 1533–1556.

Sihler KC, Napolitano L. Complications of massive transfusion. *Chest*. 2010;137:209–220.

Tanaka M, Nagasaki G, Nishikawa T. Moderate hypothermia depresses arterial baroreflex control of heart rate during, and delays its recovery after general anesthesia in humans. *Anesthesiology*. 2001;95:51–55.

C.18. What is the treatment of hypothermia?

The normal response to hypothermia is shivering, which is blocked by general anesthesia. Therefore, it is of utmost importance to prevent and treat hypothermia. Recommendations include the following:

- Increase the temperature of the operating room.
- Use a warming blanket.
- Preheat intravenous fluids.
- Pass all fluids through a warming device.
- Use low-flow anesthesia.
- Use a heat moisture exchanger in the anesthesia circuit.

C.19. What are the effects of blood transfusion on the immune system?

Blood transfusion will result in immunologic changes that can be harmful in some patients and helpful in others. This immunomodulation occurs from immune suppression. The blood components crucial to these changes are thought to be the white blood cells or plasma.

An example of a beneficial effect is the increased survival of the renal allograft in patients who had received a prior transfusion. In patients who have cancer, a possible harmful effect of immunosuppression is the increased cancer recurrence rate seen in patients who have had prior transfusion. Finally, clinical studies have demonstrated that perioperative transfusion is associated with an increased incidence of infection and sepsis.

Halel S, Nguyen D, Fontaine M, et al. Transfusion medicine. In: Lee GR, ed. *Wintrobe's Clinical Hematology*. 12th ed. Baltimore: Lippincott Williams & Wilkins; 2009: 672–721.

Landers DF. Blood transfusion-induced immunomodulation. *Anesth Analg*. 1996;82:187–204.

C.20. What are the guidelines for transfusion of blood products?

The New York Presbyterian Hospital Guidelines for blood product usage are as follows:

Red Blood cell transfusion criteria

- Hemoglobin level less than 8 g per dL and mean red cell volume within normal limit (81 to 100 fL, 70 to 125 fL for patients aged 14 years)

- Hemoglobin level less than 8 g per dL and high risk/acute bleed[1]
- Hemoglobin level less than 11 g per dL and clinically symptomatic[2]
- Hemoglobin level less than 11 g per dL and bleed more than 1 unit per 24 hours
- Any Hemoglobin level and high risk[1] and acute bleed
- Any hemoglobin level and symptomatic[2] and acute bleed
- Any hemoglobin level and bleed more than 2 units per 24 hours, or more than 15% of blood volume per 24 hours

Platelet transfusion criteria

- Platelet count less than 10,000 per μL without thrombotic thrombocytopenic purpura, idiopathic thrombocytopenic purpura, posttransfusion purpura, or hemolytic–uremic syndrome
- Platelet count less than 50,000 per μL with minor bleed, preoperative for a minor procedure or prematurity
- Platelet count less than 100,000 per μL with bleed requiring red blood cell transfusion or preoperative for a major procedure
- Bleeding with loss of 1 blood volume
- Bleeding time longer than 10 minutes
- Open heart surgery transfusion of more than mean number of red blood cell units (6 units/case)

FFP transfusion criteria

- Massive transfusion more than 6 units of red blood cells per 24 hours (more than 1 blood volume infants/children)
- Abnormal coagulation test results, with prothrombin time more than 15 seconds or partial thromboplastin time more than 45 seconds during prior 24 hours, or known congenital coagulation factor disorder and bleeding, or prophylaxis for major procedures
- Clinical evidence of abnormal bleeding from venipuncture sites or generalized oozing
- Patients with diagnosis of thrombotic thrombocytopenic purpura
- Open heart surgery transfusion of more than mean number of red blood cell units (6 units/case)

Cryoprecipitate transfusion criteria

- Massive transfusion more than 8 units of red blood cells per 24 hours
- Open heart surgery transfusion of more than mean number of red blood cell units (6 units/case)
- Bleeding or invasive procedure with hypofibrinogemia or DIC
- Deficient factor VIII or von Willebrand factor or abnormal fibrinogen and presurgical or bleed

New York Presbyterian Hospital. *Weill/Cornell Medical Center Protocols*. New York: Weill/Cornell Medical Center; 2011.

Stehling LC, Doherty DC, Faust RJ, et al. Practice guidelines for blood component therapy: a report by the ASA Task Force of Blood Components Therapy. *Anesthesiology*. 1996;84:732–747.

[1] High risk includes patients with coronary artery disease, chronic pulmonary disease, cerebrovascular disease, or congenital or acquired anemia.

[2] Symptomatic includes patients with signs or symptoms of anemia, such as tachycardia, angina, electrocardiographic changes or of neonatal respiratory distress, known hemoglobinopathy, and so forth.

C.21. What are the guidelines for the ratio of plasma/platelet transfusion to packed red blood cells in a massive transfusion?

Coagulopathy is frequently a problem for the trauma patient requiring massive transfusion. The causes are multifactorial. It is due to dilution of platelets and coagulation factors in addition to acidosis and hypothermia. Most trauma centers have implemented massive transfusion protocols that use the strategy of "hemostatic resuscitation." These protocols are highly variable, but the strategy involves minimizing aggressive crystalloid use, early resuscitation with blood products, and early administration of FFP and platelets.

At present, there are no specific guidelines to the transfusion ratio of FFP to packed red blood cells in massive transfusion. Although clearly more studies are required, the early results show an association toward increased survival when a ratio of FFP to packed red blood cells is 1:2 or higher during massive transfusion.

For platelets, in civilian clinical practice, the standard is still to use 1 six-unit pharesis pack for every 5 to 7 units of red blood cells administered. Initial data from the trauma literature suggests that increasing the platelet to packed red blood cell ratio may also potentially be beneficial.

Griffee MJ, DeLoughery TG, Thorborg PA. *Current Opinion in Anesthesiology*. 2010;23: 263–268.

Ketchum L, Hess J, Hiippala S. Indications for early fresh frozen plasma, cryoprecipitate, and platelet transfusion in trauma. *J Trauma*. 2006;60:S51–S58.

Teixara PG, Inaba K, Shilman I, et al. Impact of plasma transfusion in massively transfused trauma patients. *J Trauma*. 2009;66:693–697.

C.22. If a patient were a member of the Jehovah's Witness religious sect, would you give a blood transfusion?

Jehovah's Witnesses are best known for refusing the transfusion of blood and blood products. This belief is based on the Bible (Acts 15:28–29). In the awake and otherwise competent adult, courts have ruled that physicians cannot be held liable if they comply with a patient's directive and withhold life-saving blood administration after specific and detailed informed consent of the consequences of such an omission of treatment. The issue becomes clouded when patients are incompetent, unconscious (most Jehovah's Witnesses carry cards informing medical personnel of their religious beliefs), or minors. They believe all hope of eternal life is forfeited if they accept a transfusion. Therefore, a blood transfusion is considered a physical violation. The right of a Jehovah's Witness to refuse a blood transfusion is absolute. The courts have upheld their rights to refuse a blood transfusion. Most Witnesses take adequate legal steps to relieve the liability of the medical personnel. Most carry a medical alert card that states their wishes and they usually have made arrangements for proxy or surrogate decision makers. In addition, an open and honest avenue of communication must exist between the patient, surgeon, and anesthesiologist.

They will refuse transfusion of whole blood, packed red blood cells, white blood cells, plasma, and platelets, though they will allow the use of cardiopulmonary bypass, dialysis, or similar equipment, as well as intraoperative blood salvage in which the extracorporeal circulation is uninterrupted. Their religious understanding does not absolutely prohibit albumin, immune globulins, or hemophiliac preparations; those products must be decided on an individual basis. They accept all nonblood replacements, including nonblood colloids, crystalloids, dextrans, or oxygen-carrying blood substitutes.

An anesthesiologist may refuse to care for any patient when a procedure is elective. In an emergency situation, legal and ethical requirements apply. Conversely, any

competent adult also has the right to refuse any therapy, and to treat such a patient against that person's will is to commit battery.

Dasen KR, Niswander DG, Schlenker RE. Autologous and allogenic blood products for unanticipated massive blood loss in a Jehovah's Witness. *Anesth Analg*. 2000;90:553–555.

Gorgas DL. Transfusion therapy: blood and blood products. In: Roberts JR, ed. *Clinical Procedures in Emergency Medicine*. 5th ed. Philadelphia: WB Saunders; 2009:463–479.

Waters JH, Potter PS, Booke M. Cell salvage in the Jehovah's Witness patient. *Anesth Analg*. 2000;90:229–230.

C.23. If a child is a Jehovah's Witness and suffered from hemorrhagic shock, what would you do?

Care of minors presents the greatest concern and often leads to legal action against the parents under child-neglect status. Such actions are questioned by Jehovah's Witnesses who do seek good medical care for their children, while claiming that consideration be given to their families' religious beliefs. Doctors can appeal to the court for permission to transfuse blood to children of this sect who are underage. In an unforeseeable emergency, generally, blood may be given without consulting a court.

D. Postoperative Management

D.1. What is acute respiratory distress syndrome (ARDS)? What is transfusion-related acute lung injury (ALI)?

ARDS is an acute respiratory failure seen in patients with healthy lungs after being exposed to shock, trauma, sepsis, aspiration, transfusion, burns, or toxic inhalation. Initially, when this lung injury was thought to be related to the shock state and its resuscitation, names such as "shock lung" and "traumatic wet lung" were applied to acute respiratory insufficiently following injury. It is now recognized that many types of lung insults will result in damage to the alveolar capillary membrane, resulting in leakage of proteinaceous fluid from the intravascular space into the interstitium and subsequently into the alveolar spaces. This injury with its resulting interstitial and alveolar edema produces a clinical picture ranging from mild to severe pulmonary dysfunction that can be fatal.

ALI is characterized by impaired oxygenation, defined as a ratio of Pao_2/Fio_2 of 300 or less; bilateral pulmonary infiltrates on the frontal chest radiograph; and a pulmonary artery occlusion of 18 mm Hg or more. ARDS is defined as ALI with a Pao_2/Fio_2 ratio of 200 or less. ARDS is characterized by the following:

- Hypoxemia: Is relatively unresponsive to increasing inspired oxygen concentration
- Decreased pulmonary compliance: Clinically appears as stiff lungs
- Initially normal chest radiograph progressing to diffuse infiltrates or even to areas of complete consolidation
- Decrease in resting lung volumes, specifically functional residual capacity

Amato MB, Barbas CS, Medeiros DM, et al. Effect of a protective-ventilation strategy on mortality in the acute respiratory distress syndrome. *N Engl J Med*. 1998;338:345–354.

Drummond JC, Petrovitch CT, Lane TA. Hemostasis and transfusion medicine. In: Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:374–375.

Epstein S. Respiratory system. In: Bope ET, Kellerman R, Rakel RE, eds. *Conn's Current Therapy*. 1st ed. Philadelphia: WB Saunders; 2010:236–239.

D.2. How is ARDS treated?

The treatment of ARDS is primarily supportive. Currently, mechanical ventilation is the mainstay of supportive therapy for ARDS. The principal goal of mechanical ventilation is to minimize the deleterious effects on gas exchange. Unfortunately, mechanical ventilation has also been associated with further lung injury. Excessive alveolar volumes (volutrauma), high mean and peak airway pressures (barotrauma), and shearing forces caused by frequent collapse and opening of alveolar units are responsible for this further lung injury. Positive end-expiratory pressure is used to increase oxygenation at a fixed F_{IO_2}.

Investigators have looked at lung protection in patients with ARDS. Strategies were used to prevent ventilator-associated lung injury. Amato et al. used a strategy to limit peak inspiratory pressures by using low tidal volumes (less than 6 mL per kg) and the institution of positive end-expiratory pressure. Their strategy was associated with a lower 28-day mortality (38% vs. 71%), higher weaning rate (66% vs. 29%), and lower barotrauma rate (7% vs. 42%).

The National Heart, Lung, and Blood Institute ARDS network reported improved survival in patients using a low tidal volume strategy (6 mL per kg vs. 12 mL per kg). These investigators found a decrease in mortality of approximately 25% in the intervention group compared with the control group.

Amato MB, Barbas CS, Medeiros DM, et al. Effect of a protective-ventilation strategy on mortality in the acute respiratory distress syndrome. *N Engl J Med*. 1998;338:345–354.

Brower R, Ware L, Berthiaume Y, et al. Treatment of ARDS. *Chest*. 2001;120:4.

Epstein S. Respiratory system. In: Bope ET, Kellerman R, Rakel RE, eds. *Conn's Current Therapy*. 1st ed. Philadelphia: WB Saunders; 2010:236–239.

National Institutes of Health. *National Heart, Lung, and Blood Institute ARDS Network*; 2000.

D.3. In the recovery room, you are called to see this patient because of oliguria. How would you evaluate and treat this patient?

Oliguria is a decrease in urinary output to less than 0.5 mL/kg/hr.

ARF is a syndrome characterized by a rapid (hours to weeks) decline in glomerular filtration rate and retention of nitrogenous waste products such as blood urea nitrogen and creatinine. The kidney is remarkable in its ability to recover from almost complete loss of function. Most ARF is reversible. ARF is associated with major in-hospital morbidity and mortality. The diagnosis of ARF usually hinges on serial analysis of blood urea nitrogen and serum creatinine.

Renal failure can be divided into three categories:

Prerenal

Prerenal failure is the most common cause of ARF and is an appropriate physiologic response to renal hypoperfusion. It is usually caused by a low cardiac output resulting from hypovolemia or cardiac failure. It can be evaluated by checking the patient's heart rate, blood pressure, central venous pressure, pulmonary capillary wedge pressure, and cardiac output. If hypovolemia is the cause, then treatment would consist of a fluid bolus. If the patient is in cardiac failure, then inotropic support and diuretics could be administered. Severe renal hypoperfusion may cause ischemic acute tubular necrosis (ATN). Therefore, prerenal azotemia and ischemic ATN are part of a spectrum of manifestations of renal hypoperfusion.

Renal

Intrinsic renal failure is generally due to toxic injury or ischemia. Ischemic injury is caused by a decrease in perfusion pressure that can lead to renal cellular dysfunction.

Substances that affect renal tubular function in addition to renal blood flow can cause toxic injury. Ischemic ATN, unlike prerenal azotemia, is associated with injury to renal parenchyma and does not resolve immediately on restoration of renal perfusion. In its more extreme form, renal hypoperfusion may result in bilateral renal cortical necrosis and irreversible renal failure. Urinalysis may show cells or casts that are indicative of ARF. Intrinsic renal failure can be minor and short lived, or it can progress to chronic renal failure, depending on the severity of the insult. In the absence of congestive heart failure, use of diuretics should generally be avoided because they can exacerbate ATN. In particular, loop diuretics increase oxygen and ATP consumption at the level of the tubules.

Postrenal

Urinary tract obstruction accounts for less than 5% of cases of ARF. Urinary tract obstruction must be sought and corrected to treat possible causes of postrenal oliguria. This usually requires irrigation or changing of the Foley catheter. Consider the possibility of an intraoperative mishap causing postrenal obstruction.

Saxena R, Toto RD. Approach to the patient with kidney disease. In: Brenner BM, ed. *Brenner and Rector's the Kidney*. 8th ed. Philadelphia: Saunders; 2008:705–723.

D.4. If this patient had a crush injury and low urine output, what other concerns might you have? What if the patient has dark or "tea-colored" urine?

Leakage of myoglobin from muscles and damaged muscle cells secondary to a crush injury can result in rhabdomyolysis. Myoglobin, at high concentrations precipitates in the nephron, appearing pigmented and causing acute renal injury (ARF). The urine may look suspicious for hematuria or have a "tea colored" appearance. Rhabdomyolysis can be diagnosed by the presence of myoglobinuria or elevated serum creatine kinase levels. Preventing ARF in these patients is essential, because the development of ARF is associated with increased mortality. The treatment is hydration with large volumes of crystalloid, resulting in goal urine outputs as high as 100 to 30 mL per hour. In addition, alkinalization of the urine with agents such as bicarbonate may help by decreasing the rate of precipitation. Mannitol has also been used to induce osmotic diuresis and flush the myoglobin through the kidney. Other electrolyte abnormalities that can develop with crush injury and should be monitored for, including hyperkalemia, hyperphosphatemia, hypocalcemia, and metabolic acidosis.

Bosch X, Poch E, Grau J. Rhabdomyolysis and acute kidney injury. *N Engl J Med*. 2009;361:62–72.

Gonzalez D. Crush syndrome. *Crit Care Med*. 2005;33:S34–S34.

Saxena R, Toto RD. Approach to the patient with kidney disease. In: Brenner BM, ed. *Brenner and Rector's the Kidney*. 8th ed. Philadelphia: WB Saunders; 2008:705–723.

CHAPTER 57

Scoliosis

KATHRYN DELPIZZO AND VICTOR M. ZAYAS

A 14-YEAR-OLD GIRL

with scoliosis is scheduled for posterior spine fusion with segmental instrumentation. She has been told that her scoliosis is idiopathic. Her past medical history is unremarkable, but her mother states that she appears to get short of breath more easily than her friends when she plays basketball.

A. Medical Disease and Differential Diagnosis

1. What is scoliosis?
2. What is the most common type of scoliosis?
3. What are other types of scoliosis?
4. How is the severity of scoliosis assessed and why is the severity important?
5. What abnormalities in pulmonary function tests are most commonly seen in scoliosis? What is the cause of these abnormalities?
6. What is the most common arterial blood gas abnormality seen in scoliosis? What are possible causes for this abnormality?
7. What abnormalities of ventilatory drive may be associated with scoliosis?
8. How may the cardiovascular system be affected in patients with scoliosis?
9. What is the relationship between scoliosis and malignant hyperthermia?

B. Preoperative Evaluation and Preparation

1. What should the anesthesiologist know about the nature of the spinal curve?
2. What aspects of the history are most important?
3. What aspects of the physical examination are most important?
4. Why is a preoperative neurologic assessment important?
5. What tests would you order preoperatively?
6. What preparation should the patient have preoperatively?
7. What should you consider in ordering preoperative medications?
8. How will the surgical procedure influence the anesthetic management?

C. Intraoperative Management

1. What monitoring would you use?
2. What is the incidence of neurologic complications in scoliosis surgery and which patients are at highest risk?
3. What monitoring techniques are used to minimize neurologic complication?
4. What are somatosensory evoked potentials (SSEPs) and how are they used?
5. How reliable are SSEPs for predicting spinal injury?
6. What are motor evoked potentials (MEPs) and how are they used?
7. How is spinal cord monitoring affected by anesthetic agents? What other factors affect spinal cord monitoring?
8. What is the optimal anesthetic technique for scoliosis surgery?
9. What should be done if the SSEPs or MEPs become abnormal during surgery?
10. How is the "wake-up" test performed? What complications can occur during this test?
11. Four hours into the surgical procedure, the surgeon reports some bubbling in the thoracic portion of the wound. Shortly thereafter, end-tidal carbon dioxide decreases abruptly from 35 to 18 mm Hg, heart rate increases from 80 to 120 beats per minute, blood pressure begins to fall, and arterial saturation decreases to 90%. On auscultation through esophageal stethoscope, you hear a loud gurgling murmur. What is your diagnosis?
12. How common is significant air embolism during scoliosis surgery?
13. What should be done if an air embolus is suspected?
14. What complications occur related to positioning the patient?
15. What is transfusion-related acute lung injury (TRALI)?
16. What techniques can be used to minimize transfusion requirements?
17. What techniques would you use to produce deliberate hypotension during scoliosis surgery? What is the major concern of using this technique?

D. Postoperative Management

1. When would you extubate the patient?
2. What should be done to optimize pulmonary status?
3. What laboratory tests should be ordered postoperatively?
4. What fluid therapy would you use postoperatively?
5. What complications may occur following scoliosis surgery?
6. How would you manage this patient's pain postoperatively?

A. Medical Disease and Differential Diagnosis

A.1. What is scoliosis?

The spine normally curves posteriorly in the thoracic region and anteriorly in the lumbar region. These physiologic curves are the thoracic kyphosis and the lumbar lordosis, respectively. The spine is not normally curved when viewed from the front or back. Scoliosis refers to a lateral curvature of the spine. Curves are classified as structural or nonstructural. A nonstructural curve, such as lumbar scoliosis from a leg length discrepancy, will resolve when the patient is supine or uses a shoe lift and does not require surgical correction. In contrast, structural scoliosis lacks normal flexibility and does not correct with bending or lying supine. In addition to the lateral curvature of the spine, the vertebrae are rotated and the rib cage may be markedly deformed (Fig. 57.1). As demonstrated in the computed

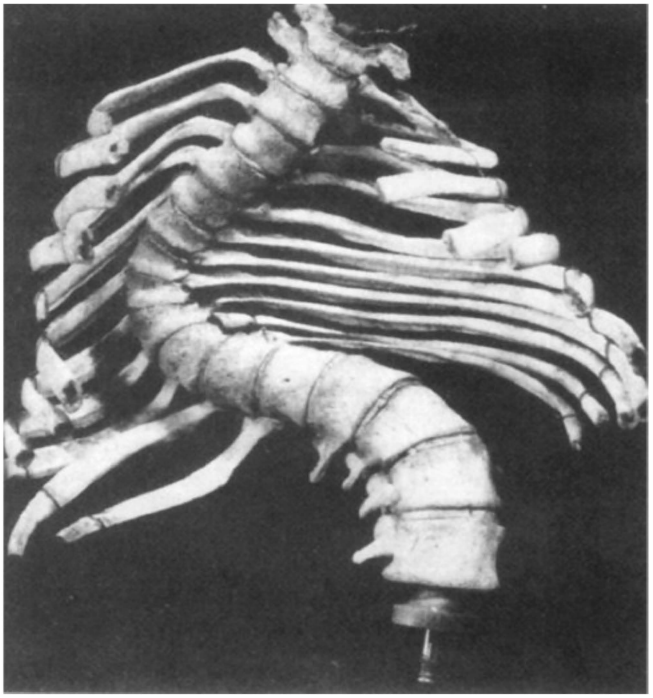


Figure 57.1 In addition to producing a lateral deformity of the spine, scoliosis also results in rotation of the vertebral bodies and significant rib cage deformity.

tomography scan image in Figure 57.2, this thoracic deformity may lead to a significant decrease in total lung volume. Particularly note the decrease in left lung volume relative to the right.

A.2. What is the most common type of scoliosis?

Idiopathic scoliosis is the most common type of scoliosis (70% of all cases) and occurs in infantile, juvenile, and adolescent forms. As the name implies, the cause is unknown, but appears to be multifactorial, including abnormalities of collagen, brainstem function, equilibrium, hormones, and growth. Genetic factors are important in its development, as evidenced by an increased incidence of scoliosis in relatives of affected patients. Recent evidence suggests that pronounced forms of scoliosis (curve greater than 11 degrees) occur only in the carriers of a mutant allele with incomplete penetrance (30% of men, 50% of women).

The prevalence of idiopathic scoliosis in large screening studies depends on the definition of scoliosis and the population screened. The prevalence of spinal curves greater than 10 degrees is 1.5% to 3%, greater than 20 degrees it is 0.3% to 0.5%, and greater than 30 degrees it is 0.2% to 0.3%. The adolescent form of idiopathic scoliosis is by far the most common in the United States. The male-to-female prevalence ratio depends in part on the age of the patient, but scoliosis requiring surgical correction is more common in women. The ratio increases with the severity of the curve, with a ratio of girls to boys at 2:1 for curves of 10 degrees, and increasing to 10:1 for curves over 30 degrees.

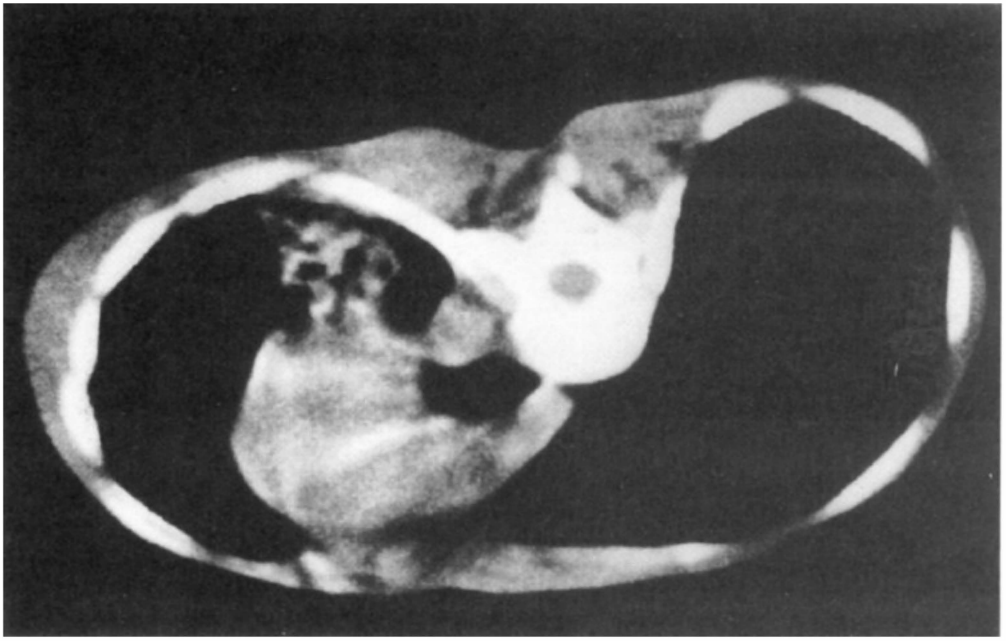


Figure 57.2 A computed tomography scan of the thorax demonstrating significant loss of lung volume resulting from the rib cage deformity.

Axenovich TI, Zaidman AM, Zorkoltseva IV, et al. Segregation analysis if idiopathic scoliosis: demonstration of a major gene defect. *Am J Med Genet* 1999;86:389–394.

Koumbourlis, Anastassios. Scoliosis and the respiratory system. *Paediatric Respiratory Reviews*. 2006;7:152–160.

Lonstein JE. Adolescent idiopathic scoliosis. *Lancet*. 1994;344:1407–1412.

Weinstein SL, ed. *The Pediatric Spine: Principles and Practice*. 2nd ed. New York: Raven Press; 2001:445–462.

Yawn BP, Yawn RA. A population-based study of school scoliosis screening. *JAMA*. 1999;282:1427–1432.

A.3. What are other types of scoliosis?

Many etiologic classifications exist for structural scoliosis. Neuromuscular scoliosis (paralytic scoliosis) may occur as a result of diseases such as cerebral palsy, muscular dystrophy, poliomyelitis, familial dysautonomia, and so on. This type of scoliosis is associated with significantly increased intraoperative blood loss compared with idiopathic scoliosis. Congenital scoliosis is the result of congenital anomalies such as hemivertebrae and fused vertebrae or ribs. Neurofibromatosis and Marfan syndrome are also associated with scoliosis. These underlying conditions may have a major impact on the anesthetic plan. The classification of structural scoliosis is as follows:

Idiopathic

- Infantile
- Juvenile
- Adolescent

Neuromuscular (Paralytic)

- Neuropathic
  - Upper motor neuron (e.g., cerebral palsy, spinal cord injury)
  - Lower motor neuron (e.g., poliomyelitis, meningomyelocoele)
  - Familial dysautonomia
- Myopathic
  - Muscular dystrophy
  - Myotonic dystrophy

Congenital

- Hemivertebrae
- Congenitally fused ribs

Neurofibromatosis

- Marfan syndrome

Mesenchymal disorders

- Ehlers-Danlos syndrome

Trauma

- Vertebral fracture or surgery
- Postthoracoplasty
- Postradiation

Bradford DS, Lonstein JE, Ogilvie JW, et al., eds. *Moe's Textbook of Scoliosis and Other Spinal Deformities*. 3rd ed. Philadelphia: WB Saunders; 1995:45–86.

A.4. How is the severity of scoliosis assessed and why is the severity important?

In 1966, the Scoliosis Research Society standardized the method for assessing the severity of scoliosis. The most common measure of severity is Cobb angle. Figure 57.3 illustrates how Cobb angle is measured on a spine radiograph. A perpendicular (*2*) is constructed from the bottom of the lowest vertebrae (*1*) whose bottom tilts toward the concavity of the curve, and another perpendicular (*4*) from the top of the highest vertebrae (*3*) whose top tilts toward the concavity. The angle (*5*) at which these perpendiculars intersect is Cobb angle. Numerous studies have documented that the more severe the thoracic curve (greater Cobb angle), the more profound the disturbance in pulmonary function. Surgical treatment is usually recommended for curves greater than 45 to 50 degrees. Curves greater than 60 degrees are usually associated with decreases in pulmonary function.

In a series of 79 patients with thoracic scoliosis, the mean Cobb angle was 45 degrees and vital capacity was decreased by an average of 22%. Figure 57.4 demonstrates that forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV_1) decrease with increasing thoracic curve severity.

Scoliosis severity and impairment of pulmonary function also increase with greater number of vertebrae involved, more cephalad location of the curve, and loss of the normal thoracic kyphosis. Severe curves have a worse prognosis because they tend to progress, and if long standing, can cause permanent damage of the lung parenchyma, respiratory failure, cor pulmonale, and death. It is important to note that patients with neuromuscular types of scoliosis may have a much more profound decrease in pulmonary function for any given curve severity.

Bradford DS, Lonstein JE, Ogilvie JW, et al. eds. *Moe's Textbook of Scoliosis and Other Spinal Deformities*. 3rd ed. Philadelphia: WB Saunders; 1995.

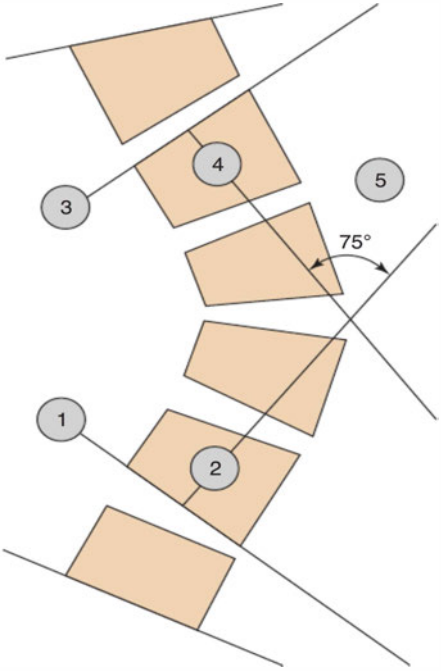


Figure 57.3 Measurement of the curve in scoliosis using Cobb angle. (Reprinted with permission from Levine DB. Scoliosis. *Curr Opin Rheumatol.* 1987;2:191.)

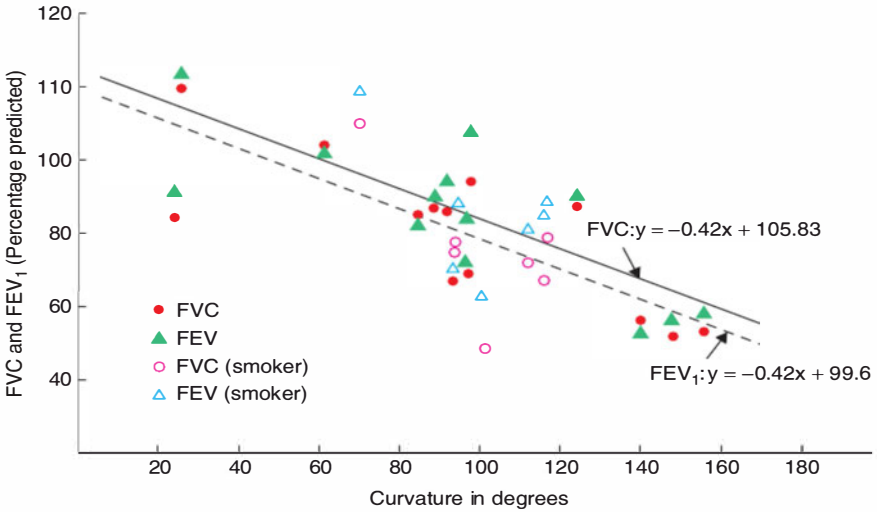


Figure 57.4 Relation between forced vital capacity (FVC), and forced expiratory volume in 1 second (FEV_1), and size of the curve in 20 patients with thoracic scoliosis. (Reproduced with permission from Weinstein SL, Zaval DC, Ponseti IV, et al. Idiopathic scoliosis. Long-term follow-up and prognosis in untreated patients. *J Bone Joint Surg.* 1981;63:702.)

Kearon C, Viviani GR, Kirkley A, et al. Factors determining pulmonary function in adolescent idiopathic thoracic scoliosis. *Am Rev Respir Dis.* 1993;148:288–294.

Levine DB. Scoliosis. *Curr Opin Rheumatol.* 1990;2:190–195.

Weinstein SL, ed. *The Pediatric Spine: Principles and Practice.* 2nd ed. New York : Raven Press; 2001:463–477.

Weinstein SL, Zaval DC, Ponseti IV, et al. Idiopathic scoliosis: long-term follow-up and prognosis in untreated patients. *J Bone Joint Surg Am.* 1981;63:702–712.

A.5. What abnormalities in pulmonary function tests are most commonly seen in scoliosis? What is the cause of these abnormalities?

A decrease in lung volumes, a restrictive pattern, is most commonly seen in thoracic scoliosis. The greatest reduction occurs in vital capacity, which is typically reduced to 60% to 80% of predicted. Total lung capacity, functional residual capacity, inspiratory capacity, and expiratory reserve volume are also decreased. An increase in residual volume has been reported in patients with congenital scoliosis and in patients with idiopathic scoliosis 3 years following corrective spine fusion.

During exercise, ventilation is adequate, but tidal volume is reduced and respiratory rate is increased. Maximal work capacity may also be decreased. Unless there is coexisting obstructive airway disease, the ratio of FEV_1/FVC is normal. Impaired respiratory muscle function also occurs in scoliosis, as evidenced by a decrease in inspiratory force to 70% of normal values. The decrease in inspiratory force is probably due to the inspiratory muscles working at a mechanical disadvantage because of the chest wall deformity.

These abnormalities in pulmonary function are usually the result of abnormal thoracic cage geometry producing a marked decrease in chest wall compliance rather than any abnormality in the lungs or respiratory muscles themselves. In dynamic magnetic resonance imaging, adolescent girls with idiopathic scoliosis and healthy controls showed no difference in diaphragmatic motion. The changes in chest wall compliance can be mimicked in normal volunteers by chest strapping. Exceptions include congenital and infantile scoliosis in which growth of the lungs may be impaired early in development by the thoracic deformity.

Barrios C, et al. Significant ventilatory function restriction in adolescents with mild or moderate scoliosis with maximal exercise tolerance test. *Spine*. 2005;30:1610–1615.

Bradford DS, Lonstein JE, Ogilvie JW, et al., eds. *Moe's Textbook of Scoliosis and Other Spinal Deformities*. 3rd ed. Philadelphia: WB Saunders; 1995:585–592.

Chu WCW, et al. Dynamic magnetic resonance imaging in assessing lung volumes, chest wall, and diaphragm motions in adolescent idiopathic scoliosis versus normal controls. *Spine.* 2006;31(19):2243–2249.

Cooper DM, Rojas JV, Mellins RB, et al. Respiratory mechanics in adolescents with idiopathic scoliosis. *Am Rev Respir Dis.* 1984;130:16–22.

Day GA, Upadhyay SS, Ho EKW, et al. Pulmonary functions in congenital scoliosis. *Spine.* 1993;19:1027–1031.

Kearon C, Viviani GR, Killian KJ. Factors influencing work capacity in adolescent idiopathic thoracic scoliosis. *Am Rev Respir Dis.* 1993;148:295–303.

Koumbourlis, Anastassios. Scoliosis and the respiratory system. *Paediatric Respiratory Reviews.* 2006;7:152–160.

A.6. What is the most common arterial blood gas abnormality seen in scoliosis? What are possible causes for this abnormality?

It has been documented that patients with thoracic scoliosis have arterial oxygen desaturation compared to normal controls. Both arterial P_{CO_2} and pH are usually

normal. Several studies have failed to show a correlation between the severity of the spinal curve and the degree of arterial oxygen desaturation.

Arterial hypoxemia is probably caused by ventilation/perfusion ($\dot{V}/\dot{Q}$) inequalities. Decreased diffusing capacity and alveolar hypoventilation may also play a role. Nevertheless, the diffusing capacity is not decreased sufficiently to be the sole cause of the hypoxemia. Similarly, alveolar ventilation at rest and during exercise is usually normal; therefore, arterial P_{CO_2} is usually normal. It has been reported that some patients have a closing capacity higher than functional residual capacity, resulting in premature airway closure during normal tidal breathing. Other studies have failed to demonstrate this finding. Some authors have reported an increase in the ratio of dead space to tidal volume (V_D/V_T), whereas other recent series have found V_D/V_T to be normal. This discrepancy may be related to the patient population studied, the severity of the scoliosis, or both. Severe and long-standing scoliosis can produce severe $\dot{V}/\dot{Q}$ abnormalities, alveolar hypoventilation, carbon dioxide retention, and more severe hypoxemia. If not surgically treated, severe scoliosis increases the risk of premature death from respiratory failure after 40 years of age. A survey of patients with respiratory failure in Sweden found that a vital capacity less than 50% of predicted and a Cobb angle greater than 100 degrees indicated an increased risk of respiratory failure.

Bergofsky EH. Respiratory failure in disorders of the thoracic cage. *Am Rev Respir Dis.* 1979;119:643–669.

Kafer ER. Respiratory and cardiovascular functions in scoliosis and the principles of anesthetic management. *Anesthesiology.* 1980;32:339–351.

Koumbourlis AC. Scoliosis and the respiratory system. *Paediatric Respiratory Reviews.* 2006;7:152–160.

Pehrsson K, Nachemson A, Olofson J, et al. Respiratory failure in scoliosis and other thoracic deformities. *Spine.* 1992;17:714–718.

Weber W, Smith JP, Briscoe WA, et al. Pulmonary function in asymptomatic adolescents with idiopathic scoliosis. *Am Rev Respir Dis.* 1975;111:389–397.

A.7. What abnormalities of ventilatory drive may be associated with scoliosis?

The slope of the ventilatory response to carbon dioxide may be decreased in patients with scoliosis. This is probably not specific to scoliosis because this response is known to be reduced in situations in which the work of breathing is increased even in the absence of a chest wall deformity. Patients with mild scoliosis have been reported to exhibit abnormal ventilatory patterns in response to hypoxemia and hypercarbia. This pattern tends to minimize the work of breathing, a higher respiratory rate, and lower tidal volume.

It has also been demonstrated that during maximal exercise, patients with mild-to-moderate scoliosis exhibit a significantly decreased ventilatory capacity, reduced exercise tolerance, and oxygen consumption despite normal pulmonary function testing at rest.

Barrios C, Perez-Encinas C, Maruenda JI, et al. Significant ventilatory restriction in adolescents with mild or moderate scoliosis during maximal exercise tolerance test. *Spine.* 2005;30:1610–1615.

Kafer ER. Respiratory and cardiovascular functions in scoliosis and the principles of anesthetic management. *Anesthesiology.* 1980;32:339–351.

Koumbourlis, Anastassios. Scoliosis and the respiratory system. *Paediatric Respiratory Reviews.* 2006;7:152–160.

Smyth RJ, Chapman KR, Wright TA, et al. Ventilatory patterns during hypoxia, hypercapnia, and exercise in adolescents with mild scoliosis. *Pediatrics.* 1986;77:692–697.

A.8. How may the cardiovascular system be affected in patients with scoliosis?

Patients with scoliosis may develop elevated pulmonary vascular resistance and pulmonary hypertension. This may result in right ventricular hypertrophy and eventually right ventricular failure. A 50-year study of untreated scoliosis demonstrated that the mortality rate of these patients was twice that of the general population and respiratory failure or right heart failure accounted for 60% of the deaths.

The increase in pulmonary vascular resistance is probably due to several factors. Hypoxemia produces pulmonary vasoconstriction, an increase in pulmonary vascular resistance, and hence an increase in pulmonary arterial pressure. Chronic hypoxemia will produce hypertensive vascular changes, and pulmonary hypertension may become irreversible. It has also been proposed that the chest wall deformity compresses some lung regions, increasing vascular resistance in those regions. Finally, if scoliosis develops in the first 6 years of life, the growth of the pulmonary vascular bed may be impaired by the chest wall deformity. Supporting this concept are reports of a decrease in the number of vascular units per lung volume in patients with scoliosis.

The most common cardiovascular abnormality in patients with scoliosis is mitral valve prolapse. Antibiotic prophylaxis should be administered before catheterization of the bladder or laryngoscopy in these patients.

Some conditions that are associated with scoliosis also affect the cardiovascular system. Patients with Duchenne muscular dystrophy develop a cardiomyopathy in the second decade of life that may not be appreciated on the basis of clinical symptoms because these patients are unable to exercise. The electrocardiogram (ECG) may reveal tachycardia, prolonged PR and QRS intervals, ST abnormalities, bundle branch block, Q waves in the left precordial leads, and tall R waves in the right precordial leads. Ejection fraction may be decreased on echocardiogram.

Patients with Marfan syndrome may have mitral and aortic insufficiency, aneurysm of the proximal ascending aorta, and abnormalities of the conduction system.

The association of scoliosis and congenital heart disease has been well established. Although no specific cardiac lesion has been identified, some series have suggested that scoliosis is more common in patients with cyanotic heart disease.

Bradford DS, Lonstein JE, Ogilvie JW, et al., eds. *Moe's Textbook of Scoliosis and Other Spinal Deformities*. 3rd ed. Philadelphia: WB Saunders; 1995:609–611.

Kafer ER. Respiratory and cardiovascular functions in scoliosis and the principles of anesthetic management. *Anesthesiology*. 1980;32:339–351.

Kawakami N, Mimatsu K, Deguchi M, et al. Scoliosis and congenital heart disease. *Spine*. 1995;20:1252–1255.

A.9. What is the relationship between scoliosis and malignant hyperthermia?

In 1970, a statistical, retrospective review of 89 patients who developed malignant hyperthermia reported that 6 of these patients had "idiopathic kyphoscoliosis." In the past 40 years, there has been no more supportive evidence of a direct relationship. Certainly, some scoliosis patients do have an increased risk of malignant hyperthermia because of their underlying disease. For example, patients with certain muscle disorders such as central core muscular dystrophy are at increased risk for developing malignant hyperthermia and also develop scoliosis (also see Chapter 53).

Britt BA, Kalow W. Malignant hyperthermia: a statistical review. *Can Anaesth Soc J*. 1970;17: 293–315.

Brownell AKW. Malignant hyperthermia: relationship to other diseases. *Br J Anaesth*. 1988;60:303–308.

B. Preoperative Evaluation and Preparation

B.1. What should the anesthesiologist know about the nature of the spinal curve?

It is important to identify the location of the curve, the age of onset, its severity, the direction of the curve, and the etiology of the scoliosis. The location of the curve is important because thoracic scoliosis is associated with pulmonary function abnormalities. Cervical scoliosis may cause difficulties in airway management and may be associated with other congenital anomalies.

The age of onset of scoliosis is of critical importance because the lung continues to grow and develop from birth until 8 years of age. The number of alveoli increases from approximately 20 million at birth to 250 million at 4 years of age. The development of significant thoracic scoliosis during this phase of rapid growth impairs lung development. A significant reduction in alveolar number has been demonstrated in patients with early-onset thoracic scoliosis, predisposing these patients to impaired gas exchange and pulmonary hypertension.

The severity of the curve is important because thoracic curves greater than 60 degrees generally produce significant decreases in pulmonary function. Curves greater than 100 degrees may be associated with significant impairment in gas exchange. Most curves in adolescent idiopathic scoliosis are convex to the right, just as most people are right-handed. A left thoracic convexity should raise the index of suspicion to look for other underlying conditions and congenital anomalies. Finally, an understanding of the etiology of the scoliosis is important because underlying conditions such as muscular dystrophy or cerebral palsy will influence anesthetic management.

Bradford DS, Lonstein JE, Ogilvie JW, et al. eds. *Moe's Textbook of Scoliosis and Other Spinal Deformities*. 3rd ed. Philadelphia: WB Saunders; 1995:585–592.

Weinstein SL, ed. *The Pediatric Spine: Principles and Practice.* 2nd ed. New York: Raven Press; 2001:421–429.

B.2. What aspects of the history are most important?

Cardiopulmonary reserve should be assessed by questioning the patient about shortness of breath, dyspnea on exertion, exercise tolerance, and so on. As a general rule, patients who can exercise normally and "keep up with friends" in vigorous activities will have good cardiopulmonary function. Pulmonary symptoms such as episodes of wheezing or cough may indicate parenchymal lung disease and alter perioperative management. Patients with muscular dystrophy, Marfan syndrome, and neurofibromatosis should be questioned about symptoms suggestive of cardiac conduction abnormalities such as palpitations or syncope.

Weinstein SL, ed. *The Pediatric Spine: Principles and Practice*. 2nd ed. New York: Raven Press; 2001:421–429.

B.3. What aspects of the physical examination are most important?

Particular emphasis in the physical examination should be directed toward the heart and lungs. Auscultation of the lungs may reveal wheezing or rales suggesting obstructive airway disease or parenchymal lung disease. On examination of the heart, in addition to auscultating for murmurs and gallops, signs of pulmonary hypertension, and right ventricular hypertrophy should be sought. Pulmonary hypertension causes

accentuation of the pulmonic component of the second heart sound and a right ventricular lift indicates right ventricular enlargement. Signs of right ventricular failure include engorged neck veins, an enlarged liver resulting from passive liver congestion, and lower extremity edema. If neurofibromatosis is suspected, the skin should be examined for the presence of *café au lait spots* or cutaneous neurofibroma. The airway should be evaluated closely for abnormalities such as cervical scoliosis, neurofibroma, or high arched palate associated with Marfan syndrome that may make endotracheal intubation difficult.

Weinstein SL, ed. *The Pediatric Spine: Principles and Practice*. 2nd ed. New York: Raven Press; 2001:421–429.

B.4. Why is a preoperative neurologic assessment important?

A preoperative neurologic assessment is important because patients who have preexisting neurologic deficits are at increased risk for developing spinal cord injury during scoliosis surgery. Furthermore, it is important to document preoperative neurologic function in order to avoid confusion about postoperative neurologic complications.

If a patient has a ventriculoperitoneal shunt for hydrocephalus, it should be evaluated preoperatively by the patient's neurosurgeon. Although rare, there have been case reports of life-threatening hydrocephalus following posterior spinal fusion in children with cerebral palsy. The shunt can malfunction during correction of the spinal deformity via disconnection, fracture, kinking, or inadequate length.

Abu-Sneineh K, Lipton GE, Gobos PG, et al. Dysfunction of a ventriculoperitoneal shunt after posterior spinal fusion in children with cerebral palsy: a report of two cases. *J Bone Joint Surg Am.* 2003;85:1119–1124.

B.5. What tests would you order preoperatively?

It is probably best to tailor diagnostic testing based on the severity of the scoliosis and underlying conditions rather than ordering a standard battery of diagnostic tests. In the current climate emphasizing medical cost containment, each institution needs to critically reassess preoperative testing. Preoperatively, this healthy 14-year-old may only need a complete blood count and the standard pregnancy test. If the history or physical examination suggests that pulmonary reserve is decreased, then standard pulmonary function testing should be considered. If vital capacity is significantly diminished, an arterial blood gas measurement is indicated. If routine pulmonary function testing reveals evidence of obstructive airway disease (a decrease in the ratio of FEV_1/FVC or a decrease in forced expiratory flow [25% to 75%]), a bronchodilator should be administered to determine if the airway obstruction is reversible.

Patients with onset of scoliosis in the first 8 years of life should have pulmonary function testing, arterial blood gas analysis, and an electrocardiogram. If the electrocardiogram reveals abnormalities such as right ventricular hypertrophy (large R in V_1 and V_2), right atrial enlargement (P_{wave} greater than 2.5 mm) or evidence of a cardiomyopathy, an echocardiogram, or even cardiac catheterization may be indicated, particularly if pulmonary hypertension is suspected.

Kafer ER. Respiratory and cardiovascular functions in scoliosis and the principles of anesthetic management. *Anesthesiology.* 1980;32:339–351.

B.6. What preparation should the patient have preoperatively?

The patient should be prepared both physiologically and psychologically for surgery and the postoperative course. First, preoperative teaching of coughing and incentive spirometry should be emphasized. Patients with evidence of parenchymal lung disease or obstructive airway disease should have aggressive pulmonary toilet or bronchodilator therapy preoperatively. Patients should know that upon awakening, they will be asked to move their extremities and follow basic commands (opening the eyes and mouth, squeezing a hand). Finally, if an intraoperative wake-up test is planned (see subsequent text), the patient should be informed and reassured that he or she will feel no pain or discomfort. It can be helpful to rehearse the wake-up test during the preoperative visit. The patient and family should understand that the wake-up test is often requested by the surgeon.

Some patients may be good candidates for preoperative autologous blood donation, particularly adult-sized patients with a high baseline hemoglobin. There is limited use in many pediatric patients because smaller children do not tolerate the phlebotomy procedure and it may not be beneficial in patients with smaller blood volumes.

B.7. What should you consider in ordering preoperative medications?

Heavy premedication and opioids are probably best avoided in patients with neuromuscular disease, evidence of pulmonary hypertension, impaired gas exchange, or markedly decreased pulmonary function. Use of an antisialagogue may be desirable because many of these surgical procedures are performed in the prone position and copious secretions may wet the tape securing the endotracheal tube and cause it to slip.

B.8. How will the surgical procedure influence the anesthetic management?

A variety of surgical procedures are commonly performed for posterior spine fusion. The blood lost during these procedures may be considerable and varies according to the procedure, the operative time, the number of segments fused, whether deliberate hypotension is used, and other factors. Even when deliberate hypotension is used, blood loss in the range of 15 to 25 mL per kg is not uncommon during uncomplicated spine fusion with Harrington rods or Cotrel-Dubousset instrumentation. This represents a blood loss of 1 to 2 L for a 70-kg patient. Postoperative bleeding may equal or exceed this, emphasizing the need for continued monitoring of these patients in the postoperative period. More extensive procedures such as combined anteroposterior spine fusion, instrumentation into the pelvis, or especially osteotomy of the spine to correct rigid deformities may be associated with blood loss exceeding the patient's own blood volume (75 mL per kg). Patients who require these more extensive procedures are frequently those with neuromuscular scoliosis (Duchenne muscular dystrophy, cerebral palsy) who may already have diminished reserves. Before the patient is taken to the operating room, the anesthesiologist should confirm that the blood bank has the anticipated blood products readily available.

Moderate third-space losses of intravascular fluid occur during scoliosis surgery. These should be replaced with balanced salt solution at a rate of 5 to 7 mL/kg/hour. This is in addition to any deficit or maintenance requirements. Procedures that are more extensive may require higher infusion rates.

The anesthesiologist should speak with the surgeon about the surgical approach and technique. The surgical plan could affect the patient's position during the case. For example, patients undergoing an anterior approach or thoracotomy may need to be positioned laterally. Another consideration is whether the surgeon requires single-lung ventilation in which case the patient may need a double-lumen endotracheal tube.

Guay J, Haig M, Lortie L, et al. Predicting blood loss in surgery for idiopathic scoliosis. *Can J Anaesth.* 1994;41:775–781.

C. Intraoperative management

C.1. What monitoring would you use?

Minimal monitoring for posterior spine fusion should include blood pressure, electrocardiogram, pulse oximetry, end-tidal carbon dioxide, esophageal stethoscope, core temperature, and spinal cord monitoring. A radial artery catheter is used for continuous monitoring of blood pressure, particularly if deliberate hypotension is planned to reduce blood loss. This will also facilitate obtaining blood samples for blood gas and hematocrit determination. All patients should have a urinary catheter placed to document urine output during and particularly after the surgical procedure. Monitoring of central filling pressures may be indicated if the expected blood loss is large, or cardiovascular disease is present or suspected. Although rarely placed in routine scoliosis surgery, a pulmonary artery catheter may be useful in patients with cardiomyopathy from Duchenne muscular dystrophy, and patients with pulmonary hypertension or right ventricular failure, in order to optimize volume replacement therapy. When placing pulmonary artery catheters in patients with pulmonary hypertension, it must be considered that the risk of pulmonary artery rupture, a complication with a mortality rate of 50%, is increased in patients with pulmonary hypertension. Neuromuscular blockade should be monitored if a balanced anesthetic technique is used.

C.2. What is the incidence of neurologic complications in scoliosis surgery and which patients are at highest risk?

In the most recent morbidity report of the Scoliosis Research Society (2006), the rate of complete or partial paraplegia was 0.26%. A study of 6,334 patients undergoing anterior, posterior, or combined anteroposterior spinal fusion reported an overall rate of spinal injury of 0.28%. Of note, combined anteroposterior procedures had a significantly higher rate of spinal cord injuries (1.12%) compared to anterior (0.0%) and posterior (0.21%) procedures.

It has been proposed that distraction of the cord and straightening of the deformity compresses the spinal cord and disrupts the arterial blood supply of the cord. The spinal cord and nerve roots may also be injured directly by hooks or instrumentation.

Prevention of neurologic complications begins with identification of the high-risk group. Patients are at increased risk for developing paraplegia if they have a severe rigid deformity (greater than 120 degrees), kyphosis, neurofibromatosis, congenital or postinfectious scoliosis, a pre-existing neurologic deficit, or more invasive instrumentation. Congenital scoliosis is associated with intraspinal anomalies, including lipomas, tethered cord, cysts, and teratomas that also increase the risk of postoperative neurologic complications. A preoperative myelogram or magnetic resonance imaging is indicated in these patients. Preoperative prophylaxis with high-dose corticosteroids should be considered for patients with a pre-existing neurologic deficit.

Cole JD, Arlet V, Donaldson W, et al. Complications in spinal fusion for adolescent idiopathic scoliosis in the new millennium: a report of the scoliosis society morbidity and mortality committee. *Spine.* 2006;31:345–349.

C.3. What monitoring techniques are used to minimize neurologic complication?

The two monitoring techniques most commonly used in the United States to monitor spinal cord function during scoliosis surgery are SSEPs and MEPs. Some centers continue to use the intraoperative wake-up test, although MEP monitoring has

replaced the routine use of the wake-up test in many centers. The intraoperative wake–up test may still be required if SSEPs or MEPs become abnormal during the surgical procedure.

Bradford DS, Lonstein JE, Ogilvie JW, et al., eds. *Moe's Textbook of Scoliosis and Other Spinal Deformities*. 3rd ed. Philadelphia: WB Saunders; 1995:471–472.

Lonstein JE. Adolescent idiopathic scoliosis. *Lancet*. 1994;344:1407–1412.

Weinstein SL, ed. *The Pediatric Spine: Principles and Practice*. 2nd ed. New York: Raven Press; 2001:1764–1765.

C.4. What are somatosensory evoked potentials (SSEPs) and how are they used?

Sensory information from the periphery passes through the posterior columns of the spinal cord on its way to the cerebral cortex. The functional integrity of this pathway can be continually assessed by monitoring SSEPs. This technique involves applying repeated electrical stimuli to a peripheral nerve (e.g., posterior tibial nerve) and measuring the evoked response over the cerebral cortex and subcortical regions using standard electroencephalogram scalp electrodes. These evoked potentials are of very low amplitude, so computer averaging or summation must be used to distinguish these potentials from background noise and the patient's electroencephalogram. A typical evoked potential waveform is shown in Figure 57.5. The time interval between electrical stimulation of peripheral nerve to recording the evoked response over the cortex is defined as the latency. An increase in the latency (slower conduction), a decrease in the amplitude, or a complete loss of the evoked potential should be considered indicative of surgical injury or ischemia until proved otherwise. It is difficult to define standard values for latency and amplitude because of the differences in recording technique among laboratories, and therefore it is important to be familiar with the normal limits for the system that is in use. In general, an increase in latency of 10% to 15% or more and a decrease in amplitude of greater than 50% should be cause for concern.

Miller RD, eds. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010: 1212–1213, 1495–1496.

Nash CL, Brown RH. Current concepts review-spinal cord monitoring. *J Bone Joint Surg Am*. 1989;71:627–630.

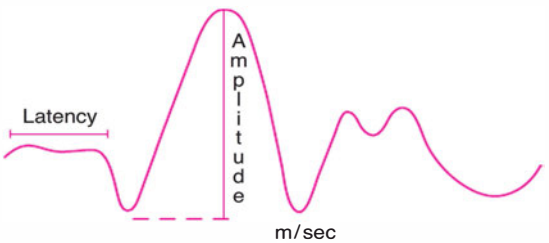


Figure 57.5 Typical somatosensory evoked potential trace. (Reprinted with permission from Cunningham JN Jr, Laschinger JC, Merkin HA, et al. Measurement of spinal cord ischemia during operations on the thoracic aorta: initial clinical experience. *Ann Surg*. 1982;196:285–296.)

C.5. How reliable are SSEPs for predicting spinal injury?

Normal intraoperative SSEPs are good predictors of normal postoperative sensory function. Although posterior (sensory) and anterior (motor) spinal injuries tend to occur together during spine surgery or spinal trauma, there have been reports of postoperative paraplegia with normal intraoperative SSEPs. This probably represents selective ischemia in the distribution of the anterior spinal artery. Sensory function and SSEPs are preserved because the posterior columns receive their blood supply from the posterior spinal arteries. For this reason, it is probably best not to rely exclusively on SSEPs to monitor spinal cord function during scoliosis surgery.

In a survey of 173 orthopedic spinal surgeons, it was found that experienced SSEP monitoring teams had fewer neurologic complications per 100 cases than teams with less experience. Neurologic defects with normal SSEPs (false negative) occurred in only 0.063% of cases.

Lesser RP, Raudzens P, Luders H, et al. Postoperative neurological deficits may occur despite unchanged intraoperative somatosensory evoked potentials. *Ann Neurol.* 1986;19:22–25.

Nash CL, Brown RH. Current concepts review-spinal cord monitoring. *J Bone Joint Surg Am.* 1989;71:627–630.

Nuwer MR, Dawson EG, Carlson LG, et al. SSEP spinal cord monitoring reduces neurologic deficits after scoliosis surgery: results of a large multicenter study. *Electroencephalogr Clin Neurophysiol.* 1995;96:6–11.

Spielholz NI, Benjamin NV, Engler GL, et al. Somatosensory evoked potentials during decompression and stabilization of the spine: methods and findings. *Spine.* 1979;4:500–505.

C.6. What are motor evoked potentials (MEPs) and how are they used?

MEPs assess the integrity of the spinal motor pathways (anterior columns). MEPs are elicited by transosseous electrical stimulation of the motor cortex using scalp electrodes or by stimulation of the anterior columns using epidural electrodes. Conduction of these stimuli through the motor pathways is monitored as peripheral nerve impulses, electromyographic signals, or actual limb movements.

In a study of 144 patients undergoing spinal deformity correction surgery, the authors report a sensitivity of 1 and a specificity of 0.97 using transcranial MEPs as the sole modality. No patient had any new neurologic deficits.

Hsu B, Cree AK, Lagopoulos J, et al. Transcranial motor-evoked potentials combined with response recording through compound muscle action potential as the sole modality of spinal cord monitoring in spinal deformity surgery. *Spine.* 2008;33:1100–1106.

C.7. How is spinal cord monitoring affected by anesthetic agents? What other factors affect spinal cord monitoring?

All anesthetic agents may affect spinal monitoring to a varying degree. This has been documented for potent inhalation agents, propofol, nitrous oxide, benzodiazepines, droperidol, etomidate, ketamine, barbiturates, and even opioids. Opioids probably have the least effect on SSEPs of all of these agents. Cortical SSEPs and MEPs are very sensitive to nitrous oxide and potent inhalational agents, whereas subcortical SSEPs are more resistant. The addition of nitrous oxide to isoflurane has been shown to have a profound effect on MEPs. MEPs are also profoundly affected by benzodiazepines and thiopental, and ketamine may enhance MEPs.

Nitrous oxide produces a decrease in amplitude in SSEPs without an increase in latency. Isoflurane, sevoflurane, halothane, and so on have similar effects on SSEPs; a dose-dependent increase in latency and decrease in amplitude. The addition of nitrous oxide appears to produce a larger decrease in amplitude than addition of 1% isoflurane or enflurane to a fentanyl-based anesthetic.

Muscle relaxants have no effect on SSEPs or MEP impulses monitored from peripheral nerves. They will affect the intensity of the motor response, which may lead to confusion in interpreting MEPs.

Although it is important to realize that anesthetic agents can affect spinal cord monitoring, excellent results can be obtained if anesthetic depth is stable. For example, it is preferable to administer opioids by continuous infusion rather than by intermittent doses. It is most important to maintain a stable anesthetic before and during periods when monitoring is critical, that is, during spine distraction or instrumentation.

A decrease in arterial pressure below levels of cerebral autoregulation, hypothermia, hematocrits below 15%, and hypoxia will affect both SSEPs and MEPs.

Bernard J, Pereon Y, Fayet G, et al. Effects of isoflurane and desflurane on neurogenic motor and somatosensory-evoked potential monitoring for scoliosis surgery. *Anesthesiology*. 1996;85:1013–1019.

Miller RD, eds. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:1502–1509.

C.8. What is the optimal anesthetic technique for scoliosis surgery?

There is no simple answer for the optimal anesthetic technique. Most patients with idiopathic scoliosis are healthy adolescents who tolerate anesthesia and surgery well, and a wide variety of techniques have been used successfully. Many healthy teenagers have a much higher tolerance for opioids and benzodiazepines and will have higher requirements for these agents intraoperatively, compared to adults. The primary concern is the ability to provide an anesthetic that is suitable for spinal cord monitoring while providing amnesia. Before the use of MEP monitoring, anesthetic techniques were tailored to facilitate the wake-up test. Monitoring of MEPs has now replaced routine use of the wake-up test in many centers. Although cortical SSEPs and MEPs may be measurable in most healthy adults receiving 50% to 70% nitrous oxide and 0.5 minimal alveolar concentration isoflurane, this combination is not suitable in small children with immature corticospinal tracts or those with pre-existing neurologic deficits. Furthermore, MEPs may be more sensitive to the combination of nitrous oxide and potent inhalational agents than cortical SSEPs.

Therefore, a typical anesthetic is a combination of a low-dose potent agent (e.g., isoflurane 0.4%) in 50% oxygen per air mixture, with a low-dose propofol infusion and primarily opioid-based intravenous anesthetic. Intravenous midazolam should be given before induction for anxiolysis and amnesia. Small doses may be repeated later if necessary. An infusion of ketamine at a low dose (0.1 to 0.2 mg/kg/hr) may improve MEP monitoring. Many centers use total intravenous anesthesia. Dexmedetomidine has been used as an adjunct in total intravenous anesthesia with minimal effect on MEPs and SSEPs. Muscle relaxants, if used, should be administered by continuous infusion and titrated to a constant train-of-four because the neuromuscular blockade will affect the intensity of the motor response. A baseline set of SSEPs and MEPs should be performed by the neuromonitoring technician as early as possible, ideally before incision, so that changes to the anesthetic or monitoring technique can be made before the most critical part of the operation (i.e., spine distraction and instrumentation).

Succinylcholine should be avoided in patients with muscle disorders. Its administration in patients with Duchenne muscular dystrophy may produce hyperkalemia, cardiac arrhythmias, myoglobinuria, or precipitate malignant hyperthermia. Patients with myotonic muscular dystrophy may exhibit sustained skeletal muscle contractions in response to succinylcholine. This may produce difficulty in ventilation and intubation.

Gibson PRJ. Anaesthesia for correction of scoliosis in children. *Anaesth Intensive Care*. 2004;32:548–559.

Tobias JD, Goble TJ, Bates G, et al. Effects of dexmedetomidine on intraoperative motor and somatosensory evoked potential monitoring during spinal surgery in adolescents. *Pediatr Anesth*. 2008;18:1082–1088.

C.9. What should be done if the SSEPs or MEPs become abnormal during surgery?

If spinal cord monitoring becomes abnormal, the anesthesiologist should ensure that oxygen delivery and spinal cord perfusion are adequate. Hypovolemia and anemia should be corrected. Arterial oxygen tension should be optimized, and arterial P_{CO_2} should be normalized if the patient is being hyperventilated. It has been reported that normalizing arterial pressure if deliberate hypotension is being used or raising arterial pressure above normal may improve spinal cord perfusion and restore SSEPs to normal. The surgeon should seek a surgical cause such as too much distraction or surgical trespass with instrumentation and correct the problem as quickly as possible. If the abnormality persists despite corrective action, a wake-up test should be performed to determine if the instrumentation should be adjusted or removed. There is evidence that the shorter the interval between detection of injury and removal of instrumentation, the better is the neurologic outcome.

Grundy BL, Nash CL, Brown CR. Arterial pressure manipulation alters spinal cord function during correction of scoliosis. *Anesthesiology*. 1981;54:249–253.

Lyon R, et al. Strategies for managing decreased motor evoked potential signals while distracting the spine during correction of scoliosis. *Journal of Neurosurgical Anesthesiology*. 2004;16(2):167–170.

C.10. How is the "wake-up" test performed? What complications can occur during this test?

The wake-up test is used to assess the integrity of the spinal motor pathways and is performed by "lightening" the depth of anesthesia sufficiently to allow the patient to follow commands. This is usually done as soon as all instrumentation is in place or if an abnormality has been detected with spinal cord monitoring. The patient is first instructed to squeeze the anesthesiologist's hand, confirming that he is responsive, and then asked to move his feet and toes. If the patient is able to squeeze his hands but unable to move his feet, the amount of spine distraction must be reduced until a safe degree of correction is achieved. When the patient moves his feet, anesthesia is quickly deepened with small doses of propofol (0.5 mg per kg). Additional short-acting benzodiazepines may be given. Recall of intraoperative events is very unusual with this technique.

The anesthesiologist should have one or two assistants available in the event the patient moves excessively during the wake-up test. Although this occurs rarely when an adequate amount of opioid has been administered, it is best to be prepared. The authors do not recommend use of opioid antagonists because of the potential for the patient to experience pain and become agitated in the prone position. If naloxone is

deemed necessary to arouse the patient, a small dose (0.3 to 0.5 mcg per kg) should be administered and repeated every 2 to 3 minutes until the respiratory depression of the opioid is reversed. It is not typically necessary to reverse neuromuscular blockade if at least three twitches are present on train-of-four stimulation.

Complications of this technique include extubation in the prone position, recall of intraoperative events, myocardial ischemia, self-injury, and dislodgment of instrumentation or intravenous access. Air embolus from open venous sinuses may occur if the patient is breathing spontaneously and inhales vigorously. It is also important to realize that the wake-up test may be performed too late, after a neurologic insult has already occurred and caused irreversible damage.

C.11. Four hours into the surgical procedure, the surgeon reports some bubbling in the thoracic portion of the wound. Shortly thereafter, end-tidal carbon dioxide decreases abruptly from 35 to 18 mm Hg, heart rate increases from 80 to 120 beats per minute, blood pressure begins to fall, and arterial saturation decreases to 90%. On auscultation through esophageal stethoscope, you hear a loud gurgling murmur. What is your diagnosis?

This constellation of symptoms strongly suggests venous air embolism. There are at least two reports indicating that air bubbling in the wound may be the first clinical sign of an air embolus before cardiovascular collapse. This is thought to occur as a result of retrograde flow of blood containing entrained air through the valveless venous system as a result of an increase in central venous pressure. Central venous pressure rises as a result of an air lock in the right heart. Positive pressure ventilation and pressure on the spine during placement of hardware may also produce bubbling of entrained air.

Adornato DC, Gildenberg PL, Ferrario CM, et al. Pathophysiology of intravenous air embolism in dogs. *Anesthesiology*. 1978;49:120–127.

Will J, Schwend RM, Albin MS, et al. Intraoperative visible bubbling of air may be the first sign of venous air embolism during posterior surgery for scoliosis. *Spine*. 2005;30:629–635.

C.12. How common is significant air embolism during scoliosis surgery?

Fortunately, clinically significant air embolism is uncommon. Nevertheless, cases of fatal air embolism have been reported during scoliosis surgery in children. Most, but not all, cases involve extensive surgical dissection with excessive bleeding. The mortality rate in the reported cases may be 50%.

C.13. What should be done if an air embolus is suspected?

If an air embolus is suspected, the surgical field should be immediately flooded with saline, ventilation begun with 100% oxygen, and intravascular fluid administered to increase central venous pressure. Air is most likely entrained from open epidural and paravertebral veins and venous sinuses in decorticated bone. Flooding the field with saline prevents air entrainment. Ventilation with 100% oxygen reduces the volume of the air embolus, particularly if nitrous oxide was administered. Hypovolemia and low central venous pressure favor air entrainment by increasing the pressure gradient between open veins and the right atrium.

If the patient requires cardiopulmonary resuscitation, placing the patient in the left lateral decubitus position during external cardiac massage may improve blood flow by breaking the air lock of the pulmonary outflow tract. Removing air through either a central catheter or by direct intracardiac aspiration has also been advocated.

McCarthy RE, Lonstein JE, Mertz JD, et al. Air embolism in spinal surgery. *J Spinal Disord.* 1990;3:1–5.

Sutherland RW, Winter RJ. Two cases of fatal air embolism in children undergoing scoliosis surgery. *Acta Anaesthesiol Scand.* 1997;41:1073–1076.

C.14. What complications occur related to positioning the patient?

If the head is not positioned carefully, pressure on the eyes may cause thrombosis of the central retinal artery producing loss of vision or blindness. The horseshoe-type head rest (Fig. 57.6) has been implicated in a number of reports of unilateral eye blindness and should be used with great caution if at all. The head should be positioned without excessive flexion or extension and in such a way that the face and eyes can be inspected easily. The position of the head and neck will move during surgical manipulation of the spine and should be inspected frequently during the procedure. It is extremely helpful to have a mirror under the patient's face that can be viewed throughout the case (Fig. 57.7). Patients with Marfan syndrome and neurofibromatosis may have abnormalities of the cervical spine and must be turned and positioned with great caution.

The upper extremities should be positioned at no more than 90 degrees of abduction to the trunk, as illustrated in Figure 57.8A. Figure 57.8B demonstrates

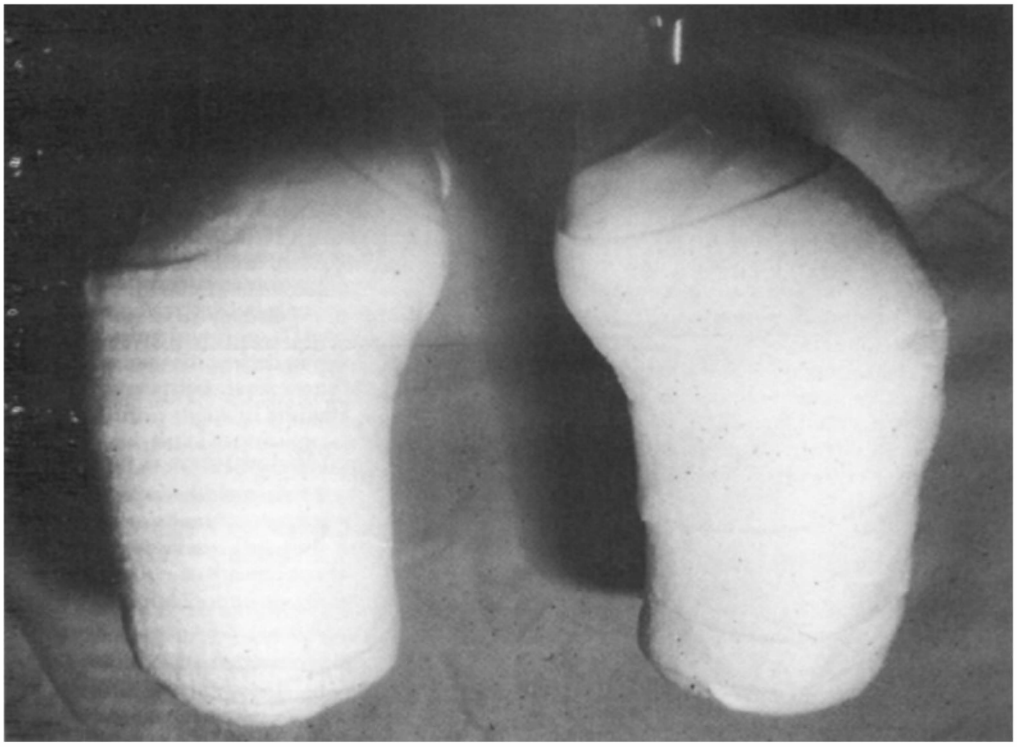


Figure 57.6 This horseshoe-type headrest has been associated with unilateral eye blindness resulting from pressure on the eye during surgery. The forehead rests on the upper portion, with the chin free in the wider, open portion.



Figure 57.7 Foam face rest with mirror.

improper arm positioning because the arms are abducted above the head. This stretches the brachial plexus and may result in a brachial plexus palsy. Both axillae should be inspected to ensure that the frame does not compress the axillary sheath. Proper positioning is shown in Figure 57.9A. Note that there is ample space between the thoracic bolster of the frame and the axilla. Figure 57.9B demonstrates improper positioning on the frame resulting in pressure on the axilla. Care should be taken to pad the ulnar nerves at the elbow. Often, the surgeons will compress or unintentionally move the upper extremities, so the arms and shoulders must be continuously monitored. Impairment of ventilation and increased bleeding from increased venous pressure may occur if the abdomen is compressed by the operating frame.

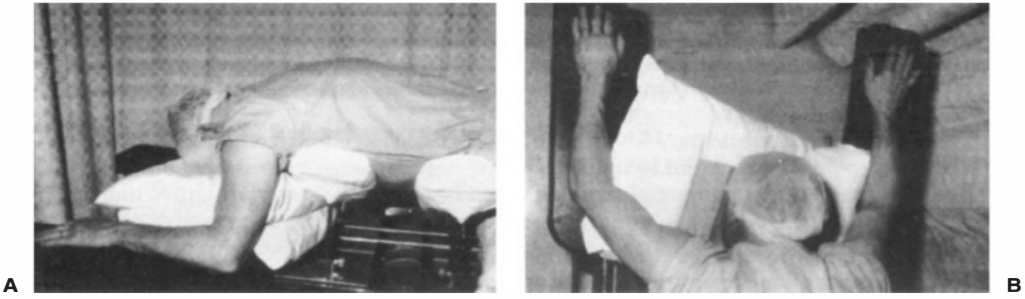


Figure 57.8 Proper arm position and improper arm position during scoliosis surgery. **A.** Degrees of abduction (relative to the trunk). **B.** Improper arm positioning with the arms abducted above the head. This results in stretching of the brachial plexus.

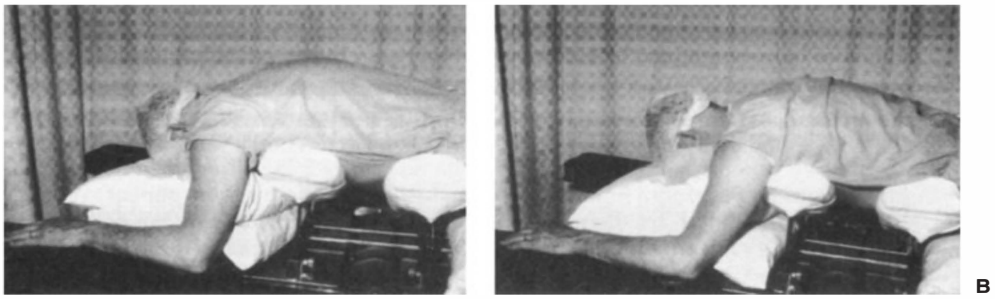


Figure 57.9 Proper and improper positioning on the four poster frame during spine surgery. **A.** Proper positioning on the frame with ample space between the axilla and the thoracic bolster of the frame. **B.** Improper positioning on the frame resulting in compression of the axillary sheath by the thoracic bolster of the frame.

Life-threatening cardiovascular events have occurred due to right ventricular outflow tract obstruction and resultant decreased venous return due to positioning of bolsters.

Neira VM, Gardin L, Ryan G, et al. A transesophageal echocardiography examination clarifies the cause of cardiovascular collapse during scoliosis urgery in a child. *Can J Anesthesia*. 2011:58:451–455.

C.15. What is transfusion-related acute lung injury (TRALI)?

TRALI is noncardiogenic pulmonary edema occurring within 1 to 6 hours of transfusion of a plasma-containing blood product. In intubated patients it presents as copious, pink, and frothy pulmonary edema fluid in the endotracheal tube. Although clinically indistinguishable from adult acute respiratory distress syndrome, TRALI is associated with a much lower mortality rate (5% to 10%). Typically, the chest radiograph and arterial oxygen saturation return to baseline within 72 hours. The exact mechanism of TRALI is unknown, but evidence points to pathologic antibodies in donor plasma causing agglutination of white blood cells on pulmonary endothelial cells. Platelet transfusions have been most commonly implicated. Therapy is supportive, similar to that for acute respiratory distress syndrome.

Popovsky MA, Davenport RD. Transfusion-related acute lung injury: femme fatale? *Transfusion*. 2001;41:312–315.

Silliman CC. Transfusion-related acute lung injury. *Transfus Med Rev*. 1999;13:177–186.

C.16. What techniques can be used to minimize transfusion requirements?

Several techniques can be used to minimize homologous blood transfusion requirements and subsequent risks such as alloimmunization, infections, immunosupression, and graft-versus-host disease. A simple and important way to minimize bleeding is to minimize intra-abdominal pressure, because any increase in abdominal pressure is transmitted to the vertebral venous plexus, increasing venous bleeding. Careful positioning will avoid external pressure on the abdomen, and muscle relaxants or deeper levels of anesthesia have been used to prevent a rise in abdominal wall tension.

Isovolemic hemodilution may also be used to minimize red cell loss during surgery. Before incision, the hematocrit is lowered 20% to 25% by removing blood aseptically and storing it in anticoagulated bags. Intravascular volume is maintained by replacing the blood with three times the volume of a balanced saline solution or an equal volume of colloid. Intraoperatively, the previously withdrawn blood is replaced as needed. Obviously this technique requires careful monitoring of intravascular volume status and hemoglobin level. Most patients will require a central venous catheter to perform this technique. Some patients who are Jehovah's Witnesses and will not accept blood transfusions may accept this type of blood conservation method because the blood can be kept in continuity with the circulation.

Salvaging of blood during the surgical procedure can play an important role as an adjunct to an autologous blood program. In our experience, 50% to 60% of the red blood cells lost can be recovered, concentrated, washed, and returned to the patient using commercially available autotransfusion devices. These red cells are obviously lacking in platelets and plasma. Some Jehovah's Witness patients may also accept this technique if the autotransfusion device is kept in continuity with the circulation.

The use of an antifibrinolytic agent such as aminocaproic acid or tranexamic acid has been shown to decrease blood loss in pediatric patients undergoing scoliosis surgery. These agents may be of particular benefit in patients with neuromuscular scoliosis such as Duchenne muscular dystrophy. These patients have significantly greater intraoperative blood loss compared to patients with idiopathic scoliosis, as much as a twofold to eightfold increased risk. The antifibrinolytic agent is administered as a loading dose followed by a continuous infusion before the activation of the fibrinolytic system, which occurs with surgical incision. It is important to administer the full loading dose before surgical incision for maximum benefit.

Deliberate hypotension has been used to decrease blood loss and improve operating conditions during spine fusion surgery. It has been shown to decrease blood loss 30% to 50% when mean arterial pressure is maintained at 50 to 60 mm Hg. (See also section C.17)

Fontana JL, Welborn L, Mongan P, et al. Oxygen consumption and cardiovascular function in children during profound intraoperative hemodilution. *Anesth Analg.* 1995;80:219–225.

Miller RD, eds. *Miller's Anesthesia*. 7th ed. Philadelphia: Churchill Livingstone; 2010:1781–1791.

Sethna NF, Zurakowski D, Brustowicz RM, et al. Ranexamic acid reduces intraoperative blood loss in pediatric patients undergoing scoliosis surgery. *Anesthesiology.* 2005;102: 727–732.

Schouten, ES, van de Pol AC, Schouten ANJ, et al. The effect of aprotinin, tranexamic acid, and aminocaproic acid on blood loss and use of blood products in major pediatric surgery: a meta-analysis. *Pediatr Crit Care Med.* 2009;10:182–190.

Florentino-Pineda I, Thompson GH, Poe-Kochert C, et al. The effect of amicar on perioperative blood loss in idiopathic scoliosis: the results of a prospective, randomized double-blind study. *Spine.* 2004;29:233–238.

Vitale MG, Privitera DM, Hiroko M, et al. Efficacy of preoperative erythropoietin administration in pediatric neuromuscular scoliosis patients. *Spine.* 2007;32:2662–2667.

C.17. What techniques would you use to produce deliberate hypotension during scoliosis surgery? What is the major concern of using this technique?

Many techniques have been used to produce deliberate hypotension. These include using high doses of potent inhalation anesthetic agents, vasodilators (sodium nitroprusside, nitroglycerin, adenosine), ganglionic blocking agents (trimethaphan), β-adrenergic blocking agents (propranolol, esmolol), angiotensin-converting enzyme inhibitors (captopril), and combinations of these agents. High doses of potent anesthetics interfere with

spinal cord monitoring and make it more difficult to perform an intraoperative wake-up test; therefore, this technique is not commonly used to produce deliberate hypotension during scoliosis surgery. Animal experiments have suggested that deliberate hypotension with trimethaphan may be associated with a decrease in spinal cord blood flow compared with sodium nitroprusside or nitroglycerin. A commonly used technique employs a short-acting vasodilator such as sodium nitroprusside and a short-acting β-adrenergic blocker such as esmolol. Mean arterial pressure can be rapidly stabilized at 50 to 65 torr and will return to normal within minutes of discontinuing these agents.

The major concern of using deliberate hypotension during scoliosis surgery is the potential for spinal cord blood flow to be compromised with resultant spinal cord injury. This is of particular concern when the spine is distracted because levels of hypotension that are considered safe under normal conditions may compromise spinal cord blood flow after spine distraction. A study in dogs demonstrated that spinal cord blood flow decreases with deliberate hypotension but returns to baseline levels after approximately 35 minutes. Therefore, it has been recommended that the spine should not be distracted for 35 minutes after the start of deliberate hypotension.

In patients at high risk for development of neurologic injury (see section C.2), it is important to balance the potential benefits of deliberate hypotension with the potential risks, and if deliberate hypotension is used, it is probably prudent to maintain mean arterial pressure no lower than 60 or 65 torr. The use of deliberate hypotension can interfere with neuromonitoring signals, particularly the MEPs. With these monitoring techniques becoming standard of care in most centers, the risks and benefits of deliberate hypotension need to be carefully considered.

Grundy BL, Nash CL, Brown CR. Arterial pressure manipulation alters spinal cord function during correction of scoliosis. *Anesthesiology.* 1981;54:249–253.

Kling TF, Ferguson NV, Leach AB, et al. The influence of induced hypotension and spine distraction on canine spinal cord blood flow. *Spine.* 1985;10:878–883.

Miller RD, eds. *Miller's Anesthesia.* 7th ed. Philadelphia: Churchill Livingstone; 2010:2065.

D. Postoperative Management

D.1. When would you extubate the patient?

The decision to continue mechanical ventilation in the postoperative period is usually made preoperatively. Most patients with adolescent idiopathic scoliosis have mild to moderate pulmonary function abnormalities and may be extubated in the operating room after they have moved all extremities to the surgeon's satisfaction. Mechanical ventilation should be continued in patients with severe restrictive lung defects (vital capacity less than 30% of predicted) or severe gas exchange abnormalities such as carbon dioxide retention. Postoperative mechanical ventilation should be considered for patients with Duchenne muscular dystrophy, familial dysautonomia, or severe cerebral palsy. Patients who are mechanically ventilated postoperatively should be managed by nurses and physicians in an intensive care setting. Patients should be sedated to tolerate the endotracheal tube, yet arousable enough to be examined every hour for potential neurologic complications. Dexmedetomidine is a good choice for short-term sedation in this population. It offers potent synergy with opioids for analgesia, and it is easily titrated for frequent wake-ups.

The parameters for extubation given below are the same as for other respiratory disorders:

- Vital capacity greater than 10 mL per kg
- Tidal volume greater than 3–6 mL per kg

- Spontaneous respiratory rate less than 30 per minute
- Negative inspiratory force greater than –30 cm H_2O

Bradford DS, Lonstein JE, Ogilvie JW, et al., eds. *Moe's Textbook of Scoliosis and Other Spinal Deformities*. 3rd ed. Philadelphia: WB Saunders; 1995:590.

Ying Yuen, VM. Dexmedetomidine: perioperative applications in children. *Pediatr Anesth.* 2010;20:256–264.

D.2. What should be done to optimize pulmonary status?

Incentive spirometry should be taught preoperatively and should be used aggressively in the postoperative period. Coughing and deep breathing should be encouraged. Patients with obstructive or reactive airway disease will benefit from bronchodilators. Opioids should be used on a patient-controlled basis with the goal of providing adequate analgesia to allow coughing and incentive spirometry without excessive respiratory depression.

D.3. What laboratory tests should be ordered postoperatively?

Upon the patient's arrival in the recovery room, blood should be sent for analysis of arterial blood gases, hematocrit, electrolytes, blood urea nitrogen, creatinine, and if blood loss has been large, platelet count, prothrombin, and partial thromboplastin time. Determination of arterial blood gases should be repeated if clinically indicated. Hyponatremia with high urinary sodium excretion has been reported following scoliosis surgery and has been attributed to the syndrome of inappropriate antidiuretic hormone secretion. These patients produce small amounts of concentrated urine and excrete large amounts of urinary sodium. Efforts to increase urine output by administration of fluid are unsuccessful and worsen the hyponatremia. Therefore, serum electrolyte concentrations should be measured at least every 12 hours for the first 24 hours and then daily for the first 2 days. Rapid decreases in serum sodium concentration or sodium concentrations less than 125 mEq per L may produce swelling of brain cells (intracellular "edema") and seizures.

Brenner BM, Rector FC, eds. *The Kidney*. 8th ed. Philadelphia: WB Saunders; 2007:494.

Lieh-Lai M, et al. Syndrome of inappropriate antidiuretic hormone secretion in children following spinal fusion. *Crit Care Med.* 1999;27(3):622–627.

D.4. What fluid therapy would you use postoperatively?

Significant losses of intravascular fluid continue to occur in the postoperative period. These should be replaced with balanced salt solution such as lactated Ringer's solution to maintain urine output at a minimum of 0.5 to 1 mL/kg/hr. Hypotonic fluids should be avoided in the first 24 to 36 hours postoperatively. The risk for postoperative hyponatremia is increased if fluid replacement is excessive or if hypotonic fluid is administered. Some authors recommend the use of colloid replacement solutions because serum albumin is often decreased following scoliosis surgery.

Brenner BM, Rector FC, eds. *The Kidney*. 8th ed. Philadelphia: WB Saunders; 2007: 495–498.

Lieh-Lai MW, Stanitski DF, Sarnaik AP, et al. Syndrome of inappropriate antidiuretic hormone secretion in children following spinal fusion. *Crit Care Med.* 1999;27(3): 622–627.

D.5. What complications may occur following scoliosis surgery?

Complications that have been reported in the postoperative period include pneumothorax, atelectasis, pleural effusion, hemothorax, thoracic duct injury, and neurologic injury. Pneumothorax may occur as a result of anterior and posterior surgical dissections, as well as secondary to central venous line placement. A chest radiograph should be obtained upon arrival in the postanesthesia care unit. Atelectasis may occur because of prolonged supine positioning and the use of opioids. Anterior spine fusion by thoracotomy poses the greatest risk of pulmonary complications. Almost 100% of patients undergoing these procedures will develop some degree of atelectasis. Incentive spirometry and deep breathing should be emphasized and may require specialized nursing care.

In addition to intraoperative neurologic complications during instrumentation or distraction of the spine, delayed paraplegia in the first few days postoperatively has been reported. This emphasizes the need for continued monitoring of neurologic status postoperatively.

In the first few postoperative days, adynamic ileus occurs commonly, and some authors recommend placement of nasogastric tubes in all patients. Less commonly, superior mesenteric artery syndrome has been reported to occur in 0.5% of patients. This presents with nausea, vomiting, and abdominal pain after a mean time of 7.2 days. This is probably due to compression of the distal third of the duodenum by the superior mesenteric artery as a result of anatomic changes related to straightening of the spine.

Altiok H, Lubicky JP, DeWald CJ, et al. The superior mesenteric artery syndrome in patients with spinal deformity. *Spine*. 2005;30:2164–2170.

Kahanowitz N, Levine DB. Iatrogenic complications of spinal surgery. *Contemp Orthop*. 1984;9:23–39.

Stockl B, Wimmer C, Innerhofer P, et al. Delayed anterior spinal artery syndrome following posterior scoliosis correction. *Eur Spine J*. 2005;14:906–909.

Weinstein SL, ed. *The Pediatric Spine: Principles and Practice*. 2nd ed. New York: Raven Press; 2001:1761–1784.

D.6. How would you manage this patient's pain postoperatively?

Most patients having scoliosis surgery are developmentally mature enough to use intravenous patient-controlled analgesia (PCA). Hydromorphone and morphine are commonly used opioids, and the PCA is usually used until postoperative day 2. Oral analgesics (e.g., oxycodone or hydrocodone with acetaminophen) should be administered once the patient is awake enough to swallow pills or elixir. Antiemetics should be given prophylactically, starting in the operating room. Serotonin receptor antagonists are the first-line treatment, but small doses of dexamethasone may also be used. Histamine-2 receptor blockers can also be helpful the first few days. A transdermal scopolamine patch may be placed preoperatively for patients with risk factors (female of childbearing age, history of motion sickness or postoperative nausea, nonsmokers).

Gan TJ. Risk factors for postoperative nausea and vomiting. *Anesth Analg*. 2006;102:1884–1898.

CHAPTER 58

Hypoxia and Equipment Failure

James B. Eisenkraft and Andrew B. Leibowitz

A 70-YEAR-OLD MAN

is to undergo cystoscopy and transurethral resection of a bladder tumor under general anesthesia through a laryngeal mask airway (LMA). He gives a history of mild asthma and uses an albuterol inhaler when necessary. Breathing room air (F_{IO_2} = 0.21), his pulse oximeter saturation reading (Spo_2) is 94%.

A. Medical Disease and Differential Diagnosis

1. What is hypoxia and what is hypoxemia?
2. Is the partial pressure of oxygen (Pao_2) in arterial blood related to age?
3. Was this patient hypoxemic?
4. What is a pulse oximeter and what is a hemoximeter?
5. How does a pulse oximeter work?
6. How is a two-wavelength pulse oximeter calibrated by the manufacturer?
7. What may affect the accuracy of a two-wavelength pulse oximeter?
8. How do the dyshemoglobins, methemoglobin (metHb) and carboxyhemoglobin (Hbco) affect Spo_2 readings?
9. What is capnometry and what is capnography? Of what value are they in patient monitoring?
10. What is meant by the term *end-tidal carbon dioxide* ($Petco_2$)?
11. What is the appearance of a normal capnogram and what is its significance?
12. What are mainstream and sidestream capnometers?
13. Show some common capnograms and provide a differential diagnosis of each event.
14. What is the arterial–alveolar difference in carbon dioxide?
15. What are some of the important safety features of the contemporary anesthesia workstation?
16. What are common sites for gas leakage?
17. How is the anesthesia machine checked for leaks?

B. Preoperative Evaluations and Preparation

1. What should be included in the equipment checkout in preparation for anesthesia?
2. What emergency equipment should be easily available to the anesthesiologist?
3. How should this patient be premedicated?

C. Intraoperative Management

1. How should this patient be monitored?
2. After uneventful inhalation mask induction, cystoscopy was begun and the Spo_2 was noted to decrease to 81% with the patient breathing an F_{IO_2} of 0.4 (oxygen at 2 L per minute and nitrous oxide at 3 L per minute). The patient developed respiratory distress. The laryngeal mask airway (LMA) was easily maintained and no gross secretions were noted. What acute diagnostic and therapeutic interventions would you perform?
3. The patient was tracheally intubated. Squeezing the reservoir bag in the circle system failed to ventilate the lungs, and a leak was noted. What are the common sites for gas leaks?

D. Postoperative Management

1. What criteria would you use for tracheal extubation?
2. What are the causes of postoperative hypoxemia?
3. What is the difference between shunt, ventilation–perfusion mismatch, and dead space?
4. What is the differential diagnosis of pulmonary edema?
5. How should the ventilator be set if mechanical ventilation is required postoperatively?
6. If this patient had acute lung injury (ALI) secondary to aspiration, beside low-tidal volume ventilation, what other changes in routine therapy should be considered?
7. What therapies that are routinely administered by the anesthesiologist may cause ALI?
8. What methods of oxygen administration may be used postoperatively?

A. Medical Disease and Differential Diagnosis

A.1. What is hypoxia and what is hypoxemia?

Hypoxia is defined as reduction of oxygen supply to tissue below physiologic levels. *Hypoxemia* is defined as deficient oxygenation of the blood. From the anesthesiologist's perspective, hypoxia is usually considered to be decreased oxygen tension (Po_2) inside the body at the tissue level or outside the body (e.g., hypoxic gas mixture), and hypoxemia is decreased oxygen tension in the arterial blood (Pao_2).

Dorland WAN. *Dorland's Illustrated Medical Dictionary*. 31st ed. Philadelphia: WB Saunders; 2007.

Wilson W. Perioperative hypoxia. In: Atlee JL, ed. *Complications in Anesthesia*. Philadelphia: WB Saunders; 1999:175.

A.2. Is partial pressure of oxygen in arterial blood (Pao_2) related to age?

Yes. There is an age-dependent decrease in the Pao_2. In 1972, Marshall and Whyche suggested the following relationship in subjects breathing room air:

$$\text{mean } Pao_2 \text{ in mm Hg} = 102 - 0.33 \text{ (age in years) mm Hg}$$

About this regression line, there are 95% confidence limits (two standard deviations [SDs]) of 10 mm Hg.

Cerveri et al. studied Pao_2 in normal nonsmoking subjects ages 40 to 90 years. They found that Pao_2 was related to age in subjects between 40 and 74 years and constructed the following reference equation:

$$Pao_2 \text{ (mm Hg)} = 143.6 - (0.39 \times \text{age}) - (0.56 \times \text{BMI}) - (0.57 \times Paco_2)$$

For subjects ≥ 75 years old, there was no correlation with age

Marshall BE, Whyche MQ. Hypoxemia during and after anesthesia. *Anesthesiology.* 1972;37:178–209.

Cerveri I, Zoia MC, Fanfulla F, et al. Reference values of arterial oxygen tension in the middle-aged and elderly. *Am J Resp and Crit Care Med.* 1995;152: 934–941.

A.3. Was this patient hypoxemic?

No. An Spo_2 reading of 94% does not signify hypoxemia. This patient is five decades older than a 20-year-old subject; therefore, his mean Pao_2 should be 5 × 5 mm Hg per decade, which is 25 mm Hg less than that (95 mm Hg) expected in a 20-year-old (see section A.2, Sorbini et al.).

$$95 - 25 = 70 \text{ mm Hg}$$

or, using the Marshall and Whyche equation (see section A.2),

$$102 - 0.33\ (70) = 79 \text{ mm Hg}$$

Assuming normal adult hemoglobin, temperature, and pH, this Pao_2 corresponds to a hemoglobin oxygen saturation of approximately 94% on the normal hemoglobin oxygen saturation versus Po_2 curve.

Although the definitions of hypoxemia given in sections A.1 and A.2 must take age into consideration, from a practical point of view, hypoxemia (in the absence of anemia) is generally considered to exist when the Pao_2 is less than 60 mm Hg, which is equivalent to a hemoglobin oxygen saturation of 90%.

Forbes RB, Layman AJ. Anticipating common intraoperative problems. In: Longnecker DE, Tinker JH, Morgan GE Jr, eds. *Principles and Practice of Anesthesiology.* 2nd ed. St. Louis: Mosby; 1998:108.

Lumb AB. *Nunn's Applied Respiratory Physiology.* 6th ed. *Philadelphia*: Elsevier Science; 2005:166.

A.4. What is a pulse oximeter and what is a hemoximeter?

The pulse oximeter is a noninvasive device that provides a real-time estimate (designated the Spo_2%) of the arterial hemoglobin saturation with oxygen. It is a transmissive oximeter in which the patient's fingertip (or other probe site; e.g., earlobe) serves as an in vivo cuvette through which light at two different wavelengths is transmitted.

If one requires an accurate determination of the arterial hemoglobin saturation with oxygen, an arterial blood sample must be drawn and analyzed in a laboratory co-oximeter, sometimes called a *hemoximeter*. The laboratory co-oximeter is a transmissive oximeter that uses six or more different wavelengths of light to measure total hemoglobin (HbTOT), oxygenated hemoglobin (Hbo_2), deoxygenated ("reduced") hemoglobin (RHb), methemoglobin (metHb), carboxyhemoglobin (HbCO), and other dyshemoglobins, such as sulfhemoglobin. Because each species of hemoglobin has a characteristic absorbance spectrum (i.e., absorbance versus wavelength), examination of a sample of blood using these six or eight wavelengths permits identification and quantification of each hemoglobin species. Conventional pulse oximeters use only two wavelengths of light; therefore, they are unable to determine all of the different hemoglobin species. Fractional saturation (Hbo_2%) is defined as $Hbo_2/(Hbo_2 + RHb + Hbco + metHb)$—that is, Hbo_2 per *total* Hb. Functional saturation (Sao_2) is defined as $Hbo_2/(Hbo_2 + RHb)$. Note that dyshemoglobins are absent from the denominator in the definition of Sao_2.

Kurki TS, Eisenkraft JB. Pulse oximetry. In: Reich DL, Kahn R, Mittnacht A, eds. *Monitoring in Anesthesia and Perioperative Care*. New York: Cambridge University Press; 2011;185–198.

A.5. How does a pulse oximeter work?

The pulse oximeter combines the technologies of spectrophotometry and optical plethysmography. In the pulse oximeter probe, light-emitting diodes transmit red light at wavelength 660 nm and infrared light at wavelength 940 nm through the fingertip or other probe site. Light that passes through the probe site is sensed by a single photodetector and expressed as absorbance at each wavelength. It can be shown that the ratio of absorbances, 660/940 nm, is related to the hemoglobin saturation with oxygen. This is spectrophotometry. Detection of pulsatile flow is by optical plethysmography. With each pulse of arterial blood, the probe site (e.g., fingertip) increases in volume, the path length of the transmitted light increases, and the absorbance of light at 660 nm and 940 nm increases. This *pulse-added* absorbance is considered to be due to the pulsatile flow of arterial blood at the probe site, so that the ratio of pulse-added absorbances, 660/940 nm, can be used to provide an estimate of hemoglobin oxygen saturation in arterial blood.

Kurki TS, Eisenkraft JB. Pulse oximetry. In: Reich DL, Kahn R, Mittnacht A., eds. *Monitoring in Anesthesia and Perioperative Care*. New York: Cambridge University Press; 2011;185–198.

A.6. How is a two-wavelength pulse oximeter calibrated by the manufacturer?

Each pulse oximeter manufacturer creates an empiric calibration algorithm, that is, one based on observations in human volunteers. The algorithm relates the average ratio of pulse-added absorbances, 660/990 nm, to the actual hemoglobin oxygen saturation in arterial blood samples drawn simultaneously and analyzed in a laboratory

hemoximeter. Observations are made with the volunteers breathing varying FIO_2 values so that data for saturations as low as 70% are obtained. The calibration algorithm that is created relates the ratio (R) of pulse-added absorbances, 660/940 nm, to the laboratory hemoximeter readings of HbO_2 or Sao_2%, depending on the pulse oximeter manufacturer. The calibration algorithm is then stored in the software of the pulse oximeter as a "lookup" table. Therefore, the pulse oximeter merely measures R, consults its "lookup" table and displays the corresponding saturation reading as Spo_2. The pulse oximeter does not actually measure saturation; it infers it from the ratio (R), and, therefore, it predicts what the laboratory hemoximeter would read if an arterial sample drawn at that moment were analyzed.

A high value for R corresponds to a low Spo_2 reading; R = 1 corresponds to an Spo_2 reading of 85%, and a low value for R corresponds to a high Spo_2 reading. Whenever the Spo_2 reading is approximately 85%, one should consider the possibility of a spurious reading as a result of the "R = 1" phenomenon. This is commonly due to malpositioning of the probe on the fingertip.

The pulse oximeter (Spo_2) reading is usually specified by the manufacturer to have an SD of ± 2%. Therefore, if the Spo_2 is 96%, there is a 68% likelihood that the true saturation (as measured by a hemoximeter) is 96 ± 2% (i.e., ± 1 SD) and a 95% likelihood that the true saturation is 96 ± 4% (i.e., ± 2 SD).

Kelleher JF, Ruff RH. The penumbra effect: Vasomotion-dependent pulse oximeter artifact due to probe malposition. *Anesthesiology*. 1989;71:787–791.

Guan Z, Baker K, Sandberg WS. Misalignment of disposable pulse oximeter probes results in false saturation readings that influence anesthetic management. *Anesth Analg*. 2009;109:1530–1533.

A.7. What may affect the accuracy of a two-wavelength pulse oximeter?

The two-wavelength pulse oximeter is most accurate when the conditions of its clinical use most closely resemble those of its calibration. Spurious readings or failure may occur during patient movement (e.g., shivering, peripheral nerve stimulation, "twitching"), presence of intense ambient light (low signal/noise ratio), electrocautery use, administration of intravenous dyes with absorbance peaks at 660 nm (e.g., methylene blue), presence of dyshemoglobins (e.g., methemoglobin, carboxyhemoglobin, and sulfhemoglobin), certain colors of nail polish, poor pulsatile flow at the probe site (e.g., hypotension, vasoconstriction, Raynaud disease), and venous pulsations (e.g., tricuspid regurgitation).

Recent improvements in pulse oximetry technology include paradigms to increase the signal/noise ratio, thereby permitting motion artifact reduction and increased sensitivity to pulsatile flow. Such pulse oximeters have significantly lower failure rates during patient movement (such as in the postanesthesia care unit) and during conditions of low flow (e.g., hypothermia).

Barker SJ. "Motion-resistant" pulse oximetry: a comparison of new and old models. *Anesth Analg*. 2002;95:967–972.

A.8. How do the dyshemoglobins, methemoglobin (metHb) and carboxyhemoglobin (Hbco) affect Spo_2 readings?

In methemoglobin, iron in the heme moiety is oxidized (such as by dapsone, benzocaine, nitric oxide, prilocaine) to the Fe^{3+} state rather than being in the normal Fe^{2+} state. Methemoglobin cannot carry oxygen and creates a physiologic anemia.

The absorbance spectrum for metHb shows it to have similar absorbances at 660 nm and 940 nm. Therefore, the more metHb that is present, the more R tends toward 1 and the Spo_2 reading toward 85%. In the presence of metHb, the Spo_2 reading overestimates the fractional saturation and underestimates the functional saturation.

In carbon monoxide (CO) poisoning, CO combines with Hb to create a physiologic hypoxemia. Hbco has a similar absorbance to Hbo_2 at 660 nm, but a very low absorbance at 940 nm. In the presence of Hbco, the Spo_2 overestimates fractional saturation and underestimates functional saturation. Although blood that is poisoned with CO appears "cherry red" to the naked eye, and therefore may look like it is fully saturated with oxygen, it is important to recognize that the ratio of absorbances 660/940 nm will suggest blood with a hemoglobin oxygen saturation in the 90s. In a subject breathing Fio_2 of 1 (when functional saturation is 100%), as the level of Hbco increases, Spo_2 decreases from close to 100% to approximately 91%.

If the presence of dyshemoglobins is suspected, arterial blood must be drawn and analyzed in a laboratory hemoximeter to obtain accurate readings of saturation.

Pulse oximetry technology continues to evolve, and multiwavelength pulse oximeters, called pulse co-oximeters, are now clinically available. One model uses eight wavelengths of light (Masimo Rainbow SET Pulse CO-Oximetry, Masimo Company, Irvine, CA), similar to the laboratory hemoximeter. This technology makes it possible to measure CO (Spco), methemoglobin (SpMet), and total hemoglobin (SpHbt), all noninvasively and in real time.

Barker SJ, Badal JJ. The measurement of dyshemoglobins and total hemoglobin by pulse oximetry. *Curr Opin Anaesthesiol*. 2008;21:805–810.

Barker SJ, Curry J, Redford D, et al. Measurement of carboxyhemoglobin and methemglobin by pulse oximetry: a human volunteer study. *Anesthesiology*. 2006;105: 892–897.

Barker SJ, Tremper KK, Hyatt J. Effects of methemoglobin on pulse oximetry and mixed venous oximetry. *Anesthesiology*. 1989;70:112–117.

A.9. What is a capnometer and what is capnography? Of what value are they in patient monitoring?

A capnometer is a device that measures the tension (in units of millimeters of mercury [mm Hg] or kilopascals [kPa]) or concentration (volumes %) of carbon dioxide (CO_2) in the gas near the patient's airway throughout the respiratory cycle. Capnography is the graphic display of the CO_2 concentration on the y-axis against time on the x-axis.

Capnometry may be achieved using different technologies that can monitor CO_2. Most capnometers now use infrared spectroscopy to measure the Pco_2 (i.e., carbon dioxide partial pressure in millimeters of mercury). A built-in barometer measures barometric pressure (P_B) so that CO_2 can also be displayed as a percentage ($Pco_2 \times 100/P_B = \%CO_2$).

Capnography is one of the American Society of Anesthesiologists' standards for basic anesthetic monitoring. ("Continual monitoring for the presence of expired carbon dioxide shall be performed unless invalidated by the nature of the patient, procedure or equipment.") It is the "gold standard" for establishing presence of ventilation.

ASA Standards for Basic Anesthetic Monitoring (approved October 21, 1986 and last amended October 20, 2010). Park Ridge, IL: American Society of Anesthesiologists; 2010.

Gravenstein JS, Jaffe MB, Paulus DA. *Capnography: Clinical Aspects*. New York: Cambridge University Press; 2004.

A.10. What is meant by the term *end-tidal carbon dioxide* (P_{ETCO_2})?

P_{ETCO_2} is the tension of CO_2 in the exhaled gas at the end of an exhalation. Because this gas originates from the alveoli, it is considered to represent the CO_2 tension in the alveolar gas (P_{ACO_2}). The P_{ACO_2} results from the combination of gases coming from ideal alveoli, where ventilation and perfusion are perfectly matched and the CO_2 concentration is the same as arterial (P_{ACO_2}), and alveolar dead space (alveoli that are ventilated but not perfused) where CO_2 concentration is the same as inspired (P_{ICO_2}) and is normally zero.

The presence of a normal capnogram and P_{ETCO_2} depends on (1) production of CO_2 by the tissues, (2) cardiac output and pulmonary blood flow to carry CO_2 to the lungs, and (3) ventilation. Monitoring of P_{ETCO_2} can be used to adjust the setting of a mechanical ventilator and monitor ventilation, as well as detect ventilator malfunctions and breathing system problems such as leaks, incompetent unidirectional valves, exhausted CO_2 absorbent, metabolic problems (e.g., malignant hyperthermia), and gas embolism.

Gravenstein JS, Jaffe MB, Paulus DA. *Capnography: Clinical Aspects*. New York: Cambridge University Press; 2004.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 6th ed. Philadelphia: Elsevier Science; 2005:157–158.

A.11. What is the appearance of a normal capnogram and what is its significance?

A typical normal capnogram (P_{CO_2} versus time) is shown in Figure 58.1. Four phases have been described.

Phase I. This is the expiratory baseline. During exhalation, CO_2–free gas from the mechanical dead space (e.g., flexible or "goose-neck" connector) and anatomic dead space (large conducting airways) flows past the CO_2 sampling port.

Phase II. This is the expiratory upstroke. It is due to CO_2 from alveoli mixed with anatomic dead space gas passing the gas sampling port and is usually a steep upslope.

Phase III. This is the expiratory or alveolar plateau and is due to alveolar CO_2.

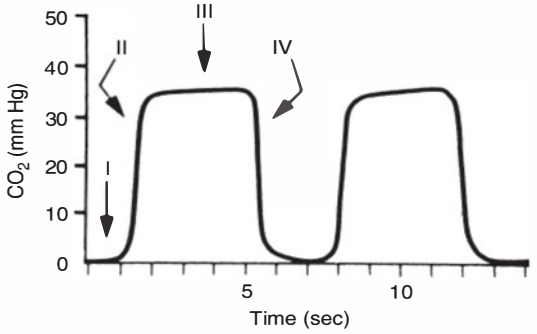


Figure 58.1 Phases of the normal capnogram. *(Phase I)* inspiratory baseline. *(Phase II)* expiratory upstroke. *(Phase III)* expiratory plateau. *(Phase IV)* inspiratory downstroke. (From Good ML. Capnography. Uses, interpretation, and pitfalls. In: *ASA Refresher Courses in Anesthesiology*. Park Ridge, IL: American Society of Anesthesiologists; 1990:179, with permission.)

In patients with healthy lungs, it is nearly horizontal, but in patients with obstructive airway disease, there is a more pronounced upward slope. The maximum expired CO_2 is usually considered as the P_{ETCO_2}.

The angle between the upstroke of phase II and the plateau of phase III is referred to as the *α angle*. The angle between phase III and IV is the *β angle*. An increase in the α angle and slope of phase III is seen commonly in acute bronchospasm. The angle usually decreases with treatment of the bronchospasm.

Phase IV. This is the inspiratory downstroke. During the commencement of inspiration, fresh (i.e., CO_2–free) gas is inhaled past the sensor and the capnogram falls sharply to baseline.

Gravenstein JS, Jaffe MB, Paulus DA. *Capnography: Clinical Aspects*. New York: Cambridge University Press; 2004.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 6th ed. Philadelphia: Elsevier Science; 2005:162.

A.12. What are mainstream and sidestream capnometers?

In a mainstream or nondiverting type of analyzer, the gas analyzer sensor is brought to the airway itself and no gas is removed from the breathing system. A cuvette with a quartz window is placed between the breathing system and the tracheal tube connector. As respired gases flow past the window in the cuvette, a beam of infrared radiation (wavelength 4.3 μm) is directed through the window. Absorbance of infrared radiation at 4.3 μm is used to measure P_{CO_2}. Advantages of the nondiverting analyzer are rapid response time, accurate waveform, and no need to scavenge gases. Disadvantages are that this additional device in the airway can be a site for a disconnect and needs sterilization (or replacement of a disposable single-use cuvette) between cases, need for heating because water vapor condensing on the window causes error, and blocking of the window by secretions or blood. Recently, a mainstream analyzer (IRMA, Phasein, Danderyd, Sweden) capable of measuring oxygen, nitrous oxide, CO_2, and all five potent inhaled anesthetics has become available.

A sidestream or diverting gas analyzer aspirates gas from the breathing circuit through a sampling adapter placed by the airway. The sampled gas passes down a sampling catheter (usually 6 to 10 ft in length) to reach the gas analyzer. Advantages of diverting analyzers are that the breathing circuit adapter is disposable. The analyzer, being remote from the airway, can be more versatile and incorporate several technologies in one "box" to analyze multiple gases (e.g., infrared analysis for CO_2, nitrous oxide, anesthetic agents; paramagnetic sensor or fuel cell for oxygen; or Raman scattering for CO_2, oxygen, agents, nitrous oxide, and nitrogen). Disadvantages of sidestream sampling analysis are slower response times, possibility of sampling leaks, errors resulting from the length of the gas sampling tube, need to scavenge gases from the analyzer after analysis, and susceptibility of the sampling tube to becoming clogged by water or secretions. Because of their versatility in regard to gas monitoring, most anesthetizing locations now use sidestream sampling analyzers.

Eisenkraft JB. Respiratory gas monitoring. In: Reich DL, Kahn R, Mittnacht A., eds. *Monitoring in Anesthesia and Perioperative Care*. New York: Cambridge University Press; 2010;150–170.

A.13. Show some common capnograms and provide a differential diagnosis of each event.

Elevated baseline equals the amount of CO_2 present in inspired gas (Fig. 58.2A).

- Capnometer not properly calibrated to zero
- Delivery of CO_2 to breathing system through fresh gas inflow
- Incompetent unidirectional valves
- Failure of CO_2 absorber (channeling, exhaustion, bypass)

Prolonged expiratory plateau and expiratory upstroke (Fig. 58.2B).

- Mechanical obstruction to exhalation
- Chronic obstructive pulmonary disease
- Bronchospasm

Dips in expiratory plateau (Fig. 58.2C[1]).

- Patient making spontaneous inspiratory effort
- "Curare cleft"

Cardiogenic oscillations if synchronized with electrocardiogram (Fig. 58.2C[2])

- Ventilator pressure relief valve perturbations

Elevated expiratory plateau (Fig. 58.2D).

- Incorrect calibration
- Increased CO_2 production/delivery versus laparoscopic CO_2 gas insufflation

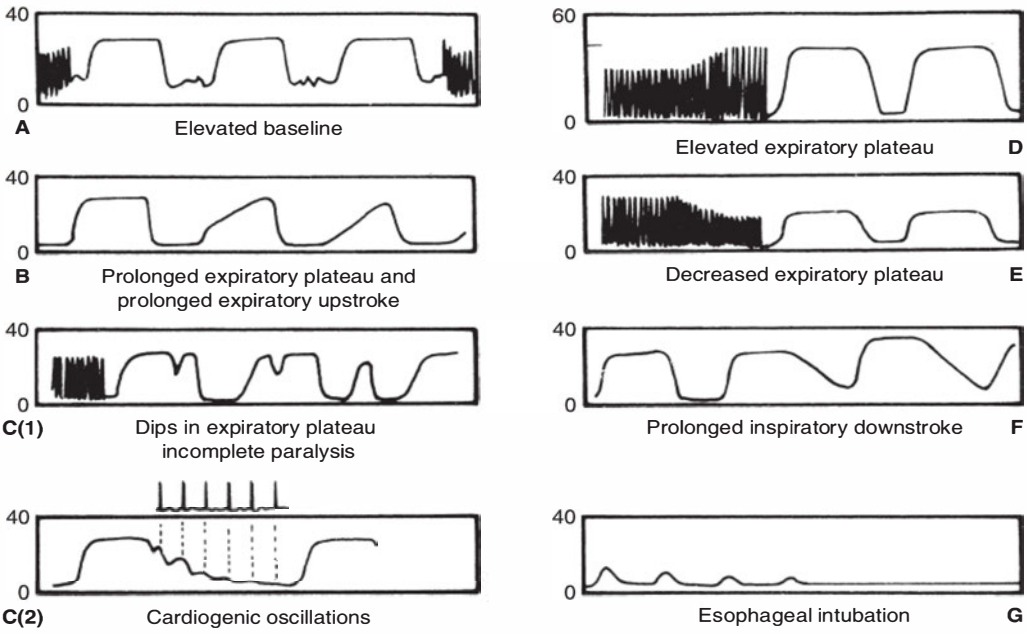


Figure 58.2 Abnormal capnograms.

- Decreased CO_2 removal
- Hypoventilation
- Leak

Decreased expiratory plateau (Fig. 58.2E).

- Incorrect calibration
- Air leak into gas sampling system
- Hyperventilation
- Decreased CO_2 production (hypothermia)
- Increased arterial–alveolar CO_2 gradient (ventilation-perfusion mismatch pulmonary embolus)

Prolonged inspiratory downstroke and raised baseline (Fig. 58.2F).

- Incompetent or missing inspiratory unidirectional valve
- Inspiratory obstruction to gas flow (e.g., kinked tracheal tube)

Esophageal intubation (Fig. 58.2G)

- As CO_2 that has been insufflated into the stomach during bag-mask ventilation, or bag-mask ventilation produced as a result of ingestion of a carbonated beverage, is washed out during esophageal ventilation, the CO_2 waveform disappears within a few breaths.

Eisenkraft JB. Respiratory gas monitoring. In: Reich DL, Kahn R, Mittnacht A., eds. *Monitoring in Anesthesia and Perioperative Care*. New York: Cambridge University Press; 2011;150–170.

A.14. What is the arterial–alveolar difference in carbon dioxide?

The arterial–alveolar difference in CO_2 is usually expressed as the difference between the arterial and P_{ETCO_2} tensions. In an ideal alveolus, the P_{aCO_2} equals P_{ACO_2} and the "P_{aCO_2}–P_{ACO_2}" difference is zero. Ventilation of unperfused alveoli leads to alveolar dead space or wasted alveolar ventilation. Because the P_{ETCO_2} comprises gas from both ideal and dead space alveoli, the "P_{aCO_2}–P_{ACO_2}" difference is a measure of alveolar dead space ventilation. For example,

$$\begin{aligned} &\text{Tidal volume} = 500\ \text{mL, anatomic dead space} = 150\ \text{mL} \\ &P_{aCO_2} = 40\ \text{mm Hg; } P_{ETCO_2} = 36\ \text{mm Hg} \\ &\text{Alveolar tidal volume} = (500 - 150) = 350\ \text{mL} \\ &\text{Ratio of } \frac{\text{Alveolar dead space}}{\text{Alveolar tidal volume}} = \frac{P_{aCO_2} - P_{ETCO_2}}{P_{aCO_2}} = \frac{40 - 36}{40} = 10\% \end{aligned}$$

Therefore, 350 ml × 10% = 35 mL wasted ventilation from each alveolar tidal volume.

$$\begin{aligned} &\text{Ideal alveolar ventilation} = (350 - 35) = 315\ \text{mL per breath} \\ &\text{In this example, physiologic dead space} = \text{anatomic} + \text{alveolar} \\ &\qquad = 150 + 35 = 185\ \text{mL per breath} \\ &\frac{\text{Physiologic dead space}}{\text{Tidal volume}} = \frac{185}{500} = 37\% \end{aligned}$$

Therefore, P_{aCO_2}–P_{ACO_2} measures alveolar dead space ventilation as a percentage of total *alveolar* ventilation. The alveolar dead space is increased by ventilation in excess of perfusion or a decrease in perfusion, such as occurs with pulmonary embolism. Shunt has minimal effect on the P_{aCO_2}–P_{ACO_2} difference.

The $Paco_2$–$Paco_2$ difference is normally 3 to 5 mm Hg in the patient under general anesthesia, but it is not constant. Therefore, although one commonly uses $Petco_2$ to noninvasively estimate $Paco_2$, only analysis of an arterial blood sample in a blood gas analyzer can provide an accurate measure of $Paco_2$, and this should be measured when critical, such as during neurosurgical anesthesia.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 6th ed. Philadelphia: Elsevier Science; 2005:120.

A.15. What are some of the important safety features of the contemporary anesthesia workstation?

Because most problems with anesthesia machines are due to use error, safety design of the contemporary workstation is at four levels.

Features intended to prevent human error

The medical gas pin index and diameter index safety systems ensure that medical gas connections are made correctly. Therefore, one cannot hang a nitrous oxide cylinder in an oxygen hanger yoke or connect a nitrous oxide hose to the oxygen pipeline inlet of the machine.

The "fail-safe" valve is a pressure-sensitive device that interrupts flow of all hypoxic gases on the machine to their flow control valves if the supply pressure of oxygen in the high-pressure system (i.e., components upstream of the oxygen flow control needle valve) falls below a threshold (20 pounds per square inch gauge [psig] in GE-Datex-Ohmeda machines; 12 psig in Dräger Narkomed machines).

When the pressure of oxygen in the high-pressure system falls below 30 psig, an oxygen supply pressure failure alarm is annunciated. The oxygen flow control knob is "touch coded"; that is, it is fluted and larger in diameter than the other gas flow control knobs and is normally located on the right of all other gas flow control valves. In the Dräger Fabius GS workstation, the gas flow controls are arranged vertically, with the oxygen flow control knob as the lowest.

Key-fill systems for anesthesia vaporizers are safety features that also decrease the likelihood of atmospheric contamination during vaporizer filling. The most important of such systems is the Saf-T-Fill system used on desflurane (Suprane) bottles and desflurane vaporizers because the filling with desflurane of a vaporizer specific for another agent could result in a lethal overdose of desflurane.

A pressure relief valve built into the machine common gas outlet, breathing system, or ventilator provides some protection against positive pressure barotrauma.

Features to correct for use error

Gas flow proportioning systems ensure a minimum oxygen concentration of 25% when nitrous oxide and oxygen are being used. Therefore, if the anesthesiologist were to accidentally attempt to increase the flow of nitrous oxide, either the oxygen flow would be increased automatically (GE-Datex-Ohmeda) or the flow of nitrous oxide would be limited according to the flow of oxygen that was set (Dräger Narkomed).

On older machines, during use of the anesthesia ventilator, changes in fresh gas flow, I:E ratio, or respiratory rate cause changes in delivered tidal volume (V_T) that might result in overventilation, underventilation, or even barotrauma. On modern systems (e.g., GE-Datex-OHMEDA S/5 ADU; GE-Datex Aisys workstations that incorporate a 7900 series ventilator with the Smart Vent feature; Dräger Fabius GS and Apollo workstations), once the ventilation parameters have been set, they are maintained because the ventilator or circuit automatically compensates for changes in gas flow settings. In the GE-Datex workstations with Smart Vent, V_T is monitored

continually by a computer. If measured V_T changes from that set to be delivered, the computer adjusts the volume delivered by the ventilator bellows. Dräger and Datascope Anestar workstations use fresh gas decoupling to maintain a constant V_T. In this system, during the inspiratory phase, a decoupling valve closes so that fresh gas entering the breathing system is directed into the reservoir bag and only gas from the ventilator is delivered to the patient. During exhalation, the ventilator chamber refills from the fresh gas flow and the fresh gas that was collected in the reservoir bag during the previous inspiration.

A vaporizer interlock system prevents the unintentional simultaneous use of more than one vaporizer.

Monitoring systems

A monitor of oxygen in the gas delivered to the patient is mandated to be enabled and the low oxygen concentration alarm is activated whenever the anesthesia workstation is capable of delivering an anesthetic gas mixture from the common gas outlet.

Other monitors in the anesthesia workstation include pressure, volume, flow, and gas composition. Some also incorporate airway gas flow monitoring. The breathing system low-pressure monitor alarm is automatically enabled when the ventilator is turned on.

Alarm systems

Contemporary workstations incorporate an integrated prioritized alarm system with visible and audible alerts when set parameter limits are exceeded.

An important safety feature of all modern machines/workstations is the preuse checkout. In 1993, the U.S. Food and Drug Administration (FDA) published anesthesia apparatus checkout recommendations. The machine should be checked by an educated user. Item no. 1 on the FDA checklist is that an alternative means to ventilate the patient's lungs should be present and functioning. Therefore, if a problem arises with the machine, the patient's lungs can be ventilated using a self-inflating resuscitation bag (e.g., Ambu bag). If a machine problem arises and the cause/remedy is not immediately obvious, one should instinctively reach for the resuscitation bag and call for help.

Recognizing that the FDA 1993 checkout recommendations cannot be applied to many of the contemporary workstations, in 2008, the American Society of Anesthesiologists published guidelines applicable to all anesthesia delivery systems so that individual departments can develop a preuse checkout that can be performed consistently and expeditiously. The 2008 guidelines are intended to provide a template for developing checkout procedures that are appropriate for each individual anesthesia machine design and practice setting. They discuss which systems and components should be checked, the checkout interval (e.g., before first case versus before every case), and who may be responsible for performing each checkout procedure—the anesthesiologist or technician (Table 58.1).

Eisenkraft JB. Anesthesia delivery system. In: Longnecker DE, Brown DL, Newman MF, et al., eds. *Anesthesiology*. New York: McGraw Hill; 2008:767–820.

Eisenkraft JB. Hazards of the anesthesia delivery system. In: Rosenblatt MA, Butterworth JB, Gross JB, eds. *ASA Refresher Courses in Anesthesiology*. Philadelphia: Lippincott-Raven, Williams & Wilkins; 2009:37:37–55.

Recommendations for Pre-Anesthesia Checkout Procedures. 2008. American Society of Anesthesiologists, Park Ridge, IL. Available at: http://www.asahq.org/clinical/FINAL CheckoutDesignguidelines02-08-2008.pdf.

Standard specification for particular requirements for anesthesia workstations and their components. West Conshohocken, PA: American Society for Testing and Materials; 2000. No. F1850-00.

A.16. What are common sites for gas leakage?

Because gas can leak from numerous points in the workstation and breathing system, the anesthesiologist must be able to trace the flow of gases from the supply and storage sources through the system components. Most commonly, leaks occur in the breathing system and low-pressure parts of the machine (i.e., components downstream of the gas flow control valves). For the breathing system, trace the flow of gas from the common gas outlet (if accessible), through the antidisconnect fitting and hose, to the breathing circuit fresh gas inlet. Trace the flow of gas past the inspiratory valve, inspiratory limb, gas sampling connector, elbow, to the tracheal tube or airway device. Common sites for leaks include a partially deflated tracheal tube cuff or a disconnection of the sidestream sampling gas analyzer sampling line. Check flow back down the expiratory limb, spirometer, expiratory valve, absorber, pressure gauge, pressure sampling lines, and any user-added components such as filters, humidifiers, and positive end-expiratory pressure (PEEP) valves. Check both the bag and the ventilator circuits for gas leaks.

Leaks in the machine low-pressure system can occur as a result of cracked rotameter flow tubes, incorrectly mounted vaporizers, vaporizer leak around agent filling device, or fracture in the gas piping. Leaks in the high-pressure system usually result from defective valves, connectors, and hanger yokes.

Brockwell RC, Andrews JJ. Inhaled anesthetic delivery systems. In: Miller RD, Erikson LI, Fleisher LA, et al., eds. *Miller's Anesthesia.* 7th ed. New York: Churchill-Livingstone; 2010:667–718.

A.17. How is the anesthesia machine checked for leaks?

Leaks in the machine low-pressure system should be tested for according to the manufacturer's specific recommendations for that particular brand and model.

In general, Dräger Narkomed machines (Narkomed 2B, Narkomed 2C, Narkomed 3, and Narkomed 4) are tested using a positive pressure leak check. In principle, the inspiratory and expiratory connections on the absorber are connected by a short length of 22-mm diameter tubing (i.e., the circle breathing system tubing is removed). The reservoir bag (usually 3 L size) is removed and a test terminal is connected to the bag mount. A short piece of plastic tubing and a sphygmomanometer bulb are connected to the test terminal. With no gases flowing and with the pop-off valve closed, the system is pressurized to 50 cm H_2O by squeezing the sphygmomanometer bulb. Pressure should not decrease by more than 20 cm H_2O in 30 seconds. In this test, the pressure is applied to all of the rigid components of the breathing system and through the fresh gas hose into the machine low-pressure system all the way back to the flow control valves. This test is then repeated with each vaporizer turned on in turn to test for leaks in each vaporizer.

Some anesthesia machines (e.g., GE-Datex-Ohmeda Modulus I, Modulus II, Excel) have a one-way outlet check valve just upstream of the common gas outlet. Other models (e.g., Modulus II Plus, Modulus CD) have no outlet check valve. The presence of an outlet check valve precludes the application of a positive pressure leak check. Whether such a valve is present, a negative pressure leak test can be used to check the low-pressure system. In this test, a suction bulb (negative pressure leak-check device) is connected to the common gas outlet. With all gas flows turned off and vaporizers off, the bulb is squeezed empty (to create a negative pressure of –65 mm Hg) and then connected to the common gas outlet of the workstation. Reexpansion of the bulb should not occur in less than 30 seconds. The test is repeated with each vaporizer turned on in turn to check for leaks in the vaporizers.

The FDA 1993 preuse checkout recommendations describe the use of the negative pressure (bulb) leak-check device and state that the bulb should not refill within 10 seconds. The anesthesiologist must understand how to perform a low-pressure

system leak check and must have the means (i.e., appropriate leak-check device) to check his or her own particular machine.

The newer electronic anesthesia workstations incorporate an automated checkout to test for leaks. The user of the workstation must understand what the automated checkout is designed to check and, more importantly, what it does not check. Even with an automated preuse checkout, some steps must be performed manually as prompted and directed by the checkout screen.

Dorsch JA, Dorsch SE. Equipment checkout and maintenance. In: *Understanding Anesthesia Equipment*. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2008:931–953.

Food and Drug Administration. Anesthesia apparatus checkout recommendations. 1993. Available at: http://vam.anest.ufl.edu/fdacheckout.html Last accessed July 1, 2011.

Myers JA, Good ML, Andrews JJ. Comparison of tests for detecting leaks in the low pressure system of anesthesia gas machines. *Anesth Analg*. 1997;84:179–184.

B. Preoperative Evaluation and Preparation

B.1. What should be included in the equipment checkout in preparation for anesthesia?

In 1993, the FDA published its *14-Step Anesthesia Apparatus Checkout Recommendations*, as follows:

This checkout, or a reasonable equivalent, should be conducted before administration of anesthesia. These recommendations are valid only for an anesthesia system that conforms to current and relevant standards and includes an ascending bellows ventilator and at least the following monitors: capnograph, pulse oximeter, oxygen analyzer, respiratory volume monitor (spirometer), and breathing system pressure monitor with high- and low-pressure alarms. This is a guideline that users are encouraged to modify to accommodate differences in equipment design and variations in local clinical practice. Such local modifications should have appropriate peer review. Users should refer to the operator's manual for the manufacturer's specific procedures and precautions, especially the manufacturer's low-pressure leak test (step no. 5).

Emergency ventilation equipment

Step 1. Verify backup ventilation equipment is available and functioning.

High-pressure system

Step 2. Check oxygen cylinder supply.
- Open oxygen cylinder and verify at least half full (approximately 1,000 psi).
- Close cylinder.

Step 3. Check central pipeline supplies.
- Check that hoses are connected and pipeline gauges read approximately 50 psi.

Low-pressure systems

Step 4. Check initial status of low-pressure system.
- Close flow control valves and turn vaporizers off.
- Check fill level and tighten vaporizer filler caps.

Step 5. Perform leak check of machine low-pressure system.
- Verify that the machine master switch and flow control valves are off.
- Attach "suction bulb" to common fresh gas outlet.
- Squeeze the bulb repeatedly until it is fully collapsed.
- Verify that the bulb stays fully collapsed for at least 10 seconds.

- Open one vaporizer at a time and repeat the tests as discussed earlier.
- Remove suction bulb, and reconnect fresh gas hose.

Step 6. Turn on machine master switch and all other necessary electrical equipment.

Step 7. Test flowmeters.
- Adjust flow of all gases through their full range, checking for smooth operation of floats and undamaged flow tubes.
- Attempt to create a hypoxic oxygen/nitrous oxide mixture and verify correct changes in flow and/or alarm.

Scavenging system

Step 8. Adjust and check scavenging system.
- Ensure proper connections between the scavenging system and both the adjustable-pressure limit (APL, or "pop-off") valve and ventilator relief valve.
- Adjust waste gas vacuum (if possible).
- Fully open APL valve and occlude Y-piece.
- With minimum oxygen flush activated, allow the scavenger reservoir bag to distend fully and then verify that the absorber pressure gauge reads less than 10 cm H_2O.

Breathing system

Step 9. Calibrate oxygen monitor.
- Ensure monitor reads 21% in room air.
- Verify low oxygen alarm is enabled and functioning.
- Reinstall sensor in circuit and flush breathing system with oxygen.
- Verify that monitor now reads more than 90%.

Step 10. Check initial status of breathing system.[1]
- Set selector switch to "bag" mode.
- Check that breathing circuit is complete, undamaged, and unobstructed.
- Verify that CO_2 absorbent is adequate.
- Install breathing circuit accessory equipment (e.g., humidifier, PEEP valve) to be used during the case.

Step 11. Perform leak check of the breathing system.
- Set all gas flows to zero (or minimum).
- Close APL (pop-off) valve and occlude Y-piece.
- Pressurize breathing system to approximately 30 cm H_2O with oxygen flush.
- Ensure that pressure remains fixed for at least 10 seconds.
- Open APL (pop-off) valve and ensure that pressure decreases.

Manual and automatic ventilation systems

Step 12. Test ventilation systems and unidirectional valves.
- Place a second breathing bag on the Y-piece.
- Set appropriate ventilator parameters for the next patient.
- Switch to automatic ventilation ("ventilator") mode.
- Fill bellows and breathing bag with oxygen flush and then turn the ventilator on.
- Set oxygen flow to minimum, and other gas flows to zero.
- Verify that during inspiration, bellows deliver appropriate tidal volume and that during expiration, bellows fill completely.
- Set fresh gas flow to approximately 5 L per minute.
- Verify that the ventilator bellows and simulated lungs fill and empty appropriately without sustained pressure at end expiration.

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[1] In step no. 10, checking adequacy of the CO_2 absorbent should include changing or hydrating it if there is any possibility that it may have become desiccated. This is because desiccated soda lime can react with desflurane, enflurane, and isoflurane to produce high levels of CO in the breathing system. Baralyme is no longer available for use as an absorbent.

- Check for proper action of unidirectional valves.
- Exercise breathing circuit accessories to ensure proper function.
- Turn ventilator off and switch to manual ventilation ("bag/APL") mode.
- Ventilate manually and ensure inflation and deflation of artificial lungs and appropriate feel of system resistance and compliance.
- Remove second breathing bag from the Y-piece.

Monitors

Step 13. Check, calibrate, and/or set alarm limits of all monitors.

- Capnometer
- Pulse oximeter
- Oxygen analyzer
- Respiratory volume monitor (spirometer)
- Pressure monitor
- High- and low-airway alarms

Final position

Step 14. Check final status of machine.

- Vaporizers off
- APL valve open
- Selector switch to "bag"
- All flowmeters to zero
- Patient suction level adequate
- Breathing system ready to use

The preanesthesia equipment checkout procedures are shown in Table 58.1.

Summary of American Society of Anesthesiologists 2008 Checkout Recommendations by Frequency and Responsible Party. Recommendations for Pre-Anesthesia Checkout Procedures. Park Ridge, IL: ASA. Available at: http://www.asahq.org/clinical/FINALCheckoutDesignguidelines02-08-2008.pdf.

B.2. What emergency equipment should be easily available to the anesthesiologist?

In checking the anesthesia machine, step no. 1 on the FDA 1993 checklist is to verify that backup ventilation equipment is available and functioning. This means a self-inflating resuscitation bag appropriate for patient size (adult versus pediatric) is present and tested. Emergency airway management equipment must be available. The latter may be stored in a "difficult airway cart."

It is also important to have available a means to perform an emergency cricothyrotomy for the "cannot intubate, cannot ventilate" scenario and a means to ventilate and oxygenate through the cricothyroid catheter, once placed. A suitable device is the Sanders injector system.

Other emergency equipment includes a working flashlight, a backup battery for any electricity-dependent workstation, an oxygen tank and regulator, a malignant hyperthermia cart, a "code" cart and defibrillator, a difficult airway cart, a fire extinguisher, knowledge of appropriate response to a fire, and an evacuation plan.

Practice Advisory for the Prevention and Management of Operating Room Fires. A Report by the American Society of Anesthesiologists Task Force on Operating Room Fires. *Anesthesiology.* 2008;108:786–801.

Surgical Fire Prevention Guide. ECRI Institute. *Health Devices.* 2009;38:314–330.

Table 58.1 Preanesthesia Equipment Checkout Procedures

TO BE COMPLETED DAILY ITEM TO BE COMPLETED		RESPONSIBLE PARTY
Item #1:	Verify auxiliary oxygen cylinder and self-inflating manual ventilation device are available and functioning.	Provider and Tech
Item #2:	Verify patient suction is adequate to clear the airway.	Provider and Tech
Item #3:	Turn on anesthesia delivery system and confirm that AC power is available.	Provider and Tech
Item #4:	Verify availability of required monitors, including alarms.	Provider and Tech
Item #5:	Verify that pressure is adequate on the spare oxygen cylinder mounted on the anesthesia machine.	Provider and Tech
Item #6:	Verify that the piped gas pressures are ≥50 psig.	Provider and Tech
Item #7:	Verify that vaporizers are adequately filled and, if applicable, that the filler ports are tightly closed.	Provider and Tech
Item #8:	Verify that there are no leaks in the gas supply lines between the flowmeters and the common gas outlet.	Provider and Tech
Item #9:	Test scavenging system function.	Provider and Tech
Item #10:	Calibrate, or verify calibration of, the oxygen. monitor and check the low oxygen alarm.	Provider and Tech
Item #11:	Verify carbon dioxide absorbent is not exhausted.	Provider and Tech
Item #12:	Breathing system pressure and leak testing.	Provider and Tech
Item #13:	Verify that gas flows properly through the breathing circuit during both inspiration and exhalation.	Provider and Tech
Item #14:	Document completion of checkout procedures.	Provider and Tech
Item #15:	Confirm ventilator settings and evaluate readiness to deliver anesthesia care. (ANESTHESIA TIME OUT)	Provider
TO BE COMPLETED PRIOR TO EACH PROCEDURE ITEM TO BE COMPLETED		**RESPONSIBLE PARTY**
Item #2:	Verify patient suction is adequate to clear the airway.	Provider and Tech
Item #4:	Verify availability of required monitors, including alarms.	Provider or Tech
Item #7:	Verify that vaporizers are adequately filled and, if applicable, that the filler ports are tightly closed.	Provider
Item #11:	Verify carbon dioxide absorbent is not exhausted.	Provider or Tech
Item #12:	Breathing system pressure and leak testing.	Provider and Tech
Item #13:	Verify that gas flows properly through the breathing circuit during both inspiration and exhalation.	Provider and Tech
Item #14:	Document completion of checkout procedures.	Provider and Tech
Item #15:	Confirm ventilator settings and evaluate readiness to deliver anesthesia care. (ANESTHESIA TIME OUT)	Provider

B.3. How should this patient be premedicated?

The goal of premedication must be established preoperatively. Commonly considered objectives listed in order of most to least common are as follows:

- Anxiolysis
- Minimization of gastric volume and acidity when "full stomach" is of concern
- Antibiotic prophylaxis (commonly administered intravenously in the operating room) before surgical incision
- Antisialagogue effect

This patient may require anxiolysis. Premedication for anxiolysis in an ambulatory patient must consider the patient's need to arrive from home and ambulate, as well as the desire for rapid return of clear mental status postoperatively. Most commonly, therefore, no agent is administered preoperatively. Alternatively, for the highly anxious patient, a small dose of a short-acting agent (e.g., lorazepam, 1 to 2 mg orally) may be administered with a few sips of water 30 to 60 minutes preoperatively.

White PF, Eng MR. Ambulatory (outpatient) anesthesia. In: Miller RD, Erikson LI, Fleisher LA, et al., eds. *Miller's Anesthesia.* 7th ed. Philadelphia: Churchill Livingstone; 2010;2419–2460.

C. Intraoperative Management

C.1. How should this patient be monitored?

The "Standards for Basic Anesthetic Monitoring" are established by the American Society of Anesthesiologists and were last amended in October 2010. In summary, they are as follows:

- *Standard I:* Qualified anesthesia personnel shall be present in the room throughout the conduct of all general anesthetics, regional anesthetics, and monitored anesthesia care.
- *Standard II:* During all anesthetics, the patient's oxygenation, ventilation, circulation, and temperature shall be continually evaluated.

Oxygenation

- *Inspired gas:* During every administration of general anesthesia using an anesthesia machine, the concentration of oxygen in the patient breathing system shall be measured by an oxygen analyzer with a low oxygen concentration limit alarm in use.*
- *Blood oxygenation:* During all anesthetics, a quantitative method of assessing oxygenation such as pulse oximetry shall be employed.* When the pulse oximeter is utilized, the variable pitch pulse tone and the low threshold alarm shall be audible to the anesthesiologist or the anesthesia care team personnel.* Adequate illumination and exposure of the patient are necessary to assess color.*

Ventilation

- Every patient receiving general anesthesia shall have the adequacy of ventilation continually evaluated. Qualitative clinical signs such as chest excursion, observation of the reservoir breathing bag, and auscultation of breath sounds are useful. Continual monitoring for the presence of expired CO_2 shall be performed unless invalidated by the nature of the patient, procedure, or equipment. Quantitative monitoring of the volume of expired gas is strongly encouraged.*
- When an endotracheal tube or laryngeal mask is inserted, its correct positioning must be verified by clinical assessment and by identification of CO_2 in the expired gas.

Continual P_{ETCO_2} analysis, in use from the time of endotracheal tube/laryngeal mask placement, until extubation/removal or initiating transfer to a postoperative care location, shall be performed using a quantitative method such as capnography, capnometry, or mass spectroscopy.* When capnography or capnometry is utilized, the P_{ETCO_2} alarm shall be audible to the anesthesiologist or the anesthesia care team personnel.*

- When ventilation is controlled by a mechanical ventilator, there shall be in continuous use a device that is capable of detecting disconnection of components of the breathing system. The device must give an audible signal when its alarm threshold is exceeded.
- During regional anesthesia and monitored anesthesia care, the adequacy of ventilation shall be evaluated by continual observation of qualitative clinical signs and/or monitoring for the presence of exhaled CO_2.

Circulation

- Every patient receiving anesthesia shall have the electrocardiogram continuously displayed from the beginning of anesthesia until preparing to leave the anesthetizing location.*
- Every patient receiving anesthesia shall have arterial blood pressure and heart rate determined and evaluated at least every 5 minutes.*
- Every patient receiving general anesthesia shall have, in addition to the above, circulatory function continually evaluated by at least one of the following: palpation of a pulse, auscultation of heart sounds, monitoring of a tracing of intra-arterial pressure, ultrasound peripheral pulse monitoring, or pulse plethysmography or oximetry.

Body temperature

- Every patient receiving anesthesia shall have temperature monitored when clinically significant changes in body temperature are intended, anticipated, or suspected.

Under extenuating circumstances, the responsible anesthesiologist may waive the requirements marked with an asterisk (*); it is recommended that when this is done, it should be so stated (including the reasons) in a note in the patient's medical record.

The reader should visit the ASA website for the most recent version of the standards: http://www.asahq.org/publicationsAndServices/standards/02.pdf

C.2. After uneventful inhalation mask induction, cystoscopy was begun and the Spo_2 was noted to decrease to 81% with the patient breathing an F_{IO_2} of 0.4 (oxygen at 2 L per minute and nitrous oxide at 3 L per minute). The patient developed respiratory distress. The laryngeal mask airway (LMA) was easily maintained and no gross secretions were noted. What acute diagnostic and therapeutic interventions would you perform?

Immediately, the patient should be examined for airway obstruction. The presence of bilateral breath sounds and the quality of those breath sounds need to be ascertained. The F_{IO_2}, $ETco_2$, heart rate, blood pressure, and Spo_2 also need to be checked. The bladder irrigation fluid intake and output, as well as the intravenous fluid intake, should be reviewed.

Therapeutically, the F_{IO_2} should be increased immediately to 1, and a change to manually assisted ventilation should be considered. If the Spo_2 does not increase rapidly in response to these interventions, tracheal intubation and initiation of positive pressure ventilation should be performed.

Dorotta I, Basali A, Ritchey M, et al. Transurethral resection syndrome after bladder perforation. *Anesth Analg.* 2003;97:1536.

C.3. The patient was tracheally intubated. Squeezing the reservoir bag in the circle system failed to inflate the lungs, and a leak was noted. What are the common sites for gas leaks?

A leak can occur anywhere in the gas circuit. One might logically check for a leak in the circuit starting from the tip of the tracheal tube and working backward toward the gas delivery system, recognizing the following common potential sites:

- Incomplete seal between the tracheal tube cuff and the trachea
- Connection between the tracheal tube and the breathing circuit (e.g., the elbow adapter)
- Spirometric and end-tidal monitoring connections at both the patient end (near the connection between the breathing circuit and tracheal tube) and the monitoring end
- Connection between inspiratory and expiratory gas hoses and the machine
- Within the low-pressure system, including the unidirectional valves, APL valve, reservoir bag or bellows housing, absorber, vaporizers, flowmeters, and scavenging system

Dorsch JA, Dorsch SE. Equipment checkout and maintenance. In: *Understanding Anesthesia Equipment*. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2008:931–953.

D. Postoperative Management

D.1. What criteria would you use for tracheal extubation?

In the operating room, traditional extubation criteria fall into two categories: global and respiratory. Global criteria include return of consciousness, demonstration of ability to protect the airway, adequate reversal of residual neuromuscular blockade, absence of hypothermia, and presence of a normal metabolic milieu (e.g., no significant anemia, acidosis, and electrolyte abnormality). Commonly applied respiratory criteria are a vital capacity greater than 15 mL per kg, a negative inspiratory force of more than –20 cm H_2O, and an Spo_2 more than 90% while breathing an F_{IO_2} less than 0.40.

Patients with a respiratory insult and the need for postoperative mechanical ventilation in the postanesthesia care unit or intensive care unit may be assessed using additional criteria. The ratio of respiratory rate to tidal volume is now widely used. This is also called the *rapid shallow breathing index* (RSBI). The idea is that slow, deep breathing during minimal respiratory support predicts successful extubation and that rapid, shallow breathing predicts probable failure. To determine this ratio, the patient is observed breathing from a T-bar, or a low level of pressure support (PS) (e.g., less than 10 cm H_2O) and the following is calculated:

$$\text{RSBI} = \text{respiratory rate (breaths per minute)}/\text{tidal volume (in liters)}$$

When the RSBI is more than 100, the implication is that the patient is exhibiting rapid, shallow breathing and will predictably fail an extubation attempt. When the RSBI is less than 100, it is assumed that the patient can breathe at a rate and tidal volume that can be easily maintained after extubation and will be adequate to maintain a normal Pao_2 and $Paco_2$. If during the period of observation while breathing from a T-bar or on PS the patient develops signs of distress such as diaphoresis, agitation, tachycardia, bradycardia, hypertension, or hypotension, the trial is abandoned and the patient is said to have had a weaning failure.

Yang KL, Tobin MJ. A prospective study of indexes predicting the outcome of trials of weaning from mechanical ventilation. *N Engl J Med.* 1991;324:1445–1450.

D.2. What are the causes of postoperative hypoxemia?

The etiology of hypoxemia can be classified physiologically or pathologically. Physiologically, all instances of hypoxemia have only four potential causes:

- Low F_{IO_2}
- Hypoventilation (which will also be associated with an increased P_{aCO_2})
- Ventilation–perfusion mismatch
- Shunt

Pathologically, common etiologies likely to present postoperatively include airway obstruction, atelectasis (especially with upper abdominal retraction and Trendelenburg positioning), right mainstem intubation, aspiration, pulmonary edema, and pulmonary embolus.

Nicholau D. The postoperative care unit. In: Miller RD, Erikson LI, Fleisher LA, et al., eds. *Miller's Anesthesia.* 7th ed. Philadelphia: Churchill Livingstone; 2010:2707–2728.

D.3. What is the difference between shunt, ventilation–perfusion mismatch, and dead space?

The relative quantity of perfusion and ventilation defines these terms. A normal lung has a small portion in which perfusion and ventilation are perfectly matched. Two extreme conditions may exist at either end of the spectrum of perfectly matched perfusion and ventilation; those extremes are shunt and dead space ventilation.

In a shunt, the alveolus is perfused, but it is not ventilated. The physiologic result is hypoxemia. This is characterized by a failure of the P_{aO_2} to rise despite an increase in the F_{IO_2}. Hypoxemia caused by small amounts of shunted blood (i.e., less than 20% of cardiac output) is easily overcome by increasing the F_{IO_2}. This is because the blood that is not shunted will contain enough "extra" dissolved oxygen to make up for the deficit that the shunted blood contributes to the combined total of blood oxygen content. Once the shunt fraction approaches 0.3 (30%), increasing the F_{IO_2} even to 1 will not be effective in preventing hypoxemia. The term *venous admixture* is often used synonymously for shunt.

In dead space, the alveolus is ventilated, but it is not perfused; hence, the alveolar space is essentially "dead." The physiologic result is hypercarbia. This is characterized by a failure to maintain a normal P_{aCO_2} despite an increase in minute ventilation (i.e., tidal volume × respiratory rate).

Ventilation–perfusion mismatch is the term applied to any condition that is not a perfect match—that is, shunt or dead space. The physiologic result is a variable combination of hypoxemia and hypercarbia. The resultant degree of hypoxemia and hypercarbia depends on the relative contribution of partial shunt and dead space.

Benatar SR, Hewlett AM, Nunn JF. The use of iso-shunt lines for the control of oxygen therapy. *Br J Anaesth.* 1973;45:711–718.

Lumb AB. *Nunn's Applied Respiratory Physiology.* 6th ed. Philadelphia: Elsevier Science, 2005:122–126.

Petros AJ, Doré CJ, Nunn JF. Modification of the iso-shunt lines for low inspired oxygen concentrations. *Br J Anaesth.* 1994;72:515–522.

D.4. What is the differential diagnosis of pulmonary edema?

Pulmonary edema is usually thought to be either cardiac or noncardiac in etiology. The differential diagnosis of pulmonary edema is shown in Table 58.2.

Conditions that physiologically result from an increase in the pressure within the vessel that cause transudation of fluid from inside the vessel to outside the vessel are traditionally termed *congestive heart failure* (CHF). CHF will be associated with a diminution of cardiac function and an increase in the left ventricular end-diastolic pressure.

A decrease in the pressure outside of the vessel may also result in the net movement of fluid from inside to outside. The classic example of this would be negative pressure pulmonary edema, a condition seen in young patients who are inspiring against a closed glottis.

A change in the permeability of the vessel wall is the major cause of pulmonary edema seen in acute lung injury (ALI) and acute respiratory distress syndrome (ARDS). These conditions require a history of exposure to a risk factor, the development of bilateral infiltrates on chest radiography, and documentation of the absence of heart failure either by echocardiogram or pulmonary artery catheterization. Risk factors for ALI and ARDS include aspiration, long bone fracture, transfusion-related acute lung injury, pancreatitis, inhalational injury, and sepsis (Table 58.2).

In this patient, acute fluid overload from absorption of bladder irrigation fluid should be considered. Physiologically, this picture resembles CHF and will respond to treatment with diuretics.

Bittner EA, Grecu L, George E. Postoperative complications. In: Longnecker DE, Brown D, Newman M, et al., eds. *Anesthesiology*. New York: McGraw Hill; 2007:1700–1715.

Dorotta I, Basali A, Ritchey M, et al. Transurethral resection syndrome after bladder perforation. *Anesth Analg*. 2003;97:1536.

D.5. How should the ventilator be set if mechanical ventilation is required postoperatively?

Parameters that must be set include the mode, respiratory rate, tidal volume, PEEP, and F_{IO_2}.

Patients with an acute need for mechanical ventilation should be given full support with the mode set as volume control, with which all breaths are delivered by the ventilator. Other modes to be considered as the patient improves include synchronized intermittent mandatory ventilation, PS, and combinations of synchronized intermittent mandatory ventilation and PS.

Tidal volume has traditionally been set at 10 mL per kg. Normally, during spontaneous ventilation, the respiratory rate is 12 to 16 breaths per minute and the tidal volume is 6 mL per kg. However, during spontaneous ventilation, there are yawns and sighs that prevent atelectasis. Yawns and sighs are not administered during routine mechanical ventilation. Therefore, standard mechanical ventilation settings use a lower respiratory rate and higher tidal volume than spontaneous values, resulting in the same minute ventilation and no need for sigh (150% of V_T) breaths.

Traditional mechanical ventilation has been recognized as a potential cause of morbidity and mortality when applied to injured lungs. The excessive V_T is thought to cause alveolar injury and worsen lung damage (i.e., volutrauma). This should be distinguished from the more easily recognized concern of pneumothorax, resulting from ventilation of stiff lungs with high inflation pressures, commonly referred to as *barotrauma*. Hence, the current recommendation in ALI and ARDS is that the V_T be set at 6 mL per kg of premorbid weight. Additionally, the peak inspiratory pressure should ideally be less than 35 cm H_2O. This may result in CO_2 retention, but if the

Table 58.2 Differential Diagnosis of Pulmonary Edema

CONDITION	PATHOPHYSIOLOGY	SAMPLE CAUSE
Congestive heart failure	↑ Filling pressure, ↓ cardiac output	Myocardial infarction
Negative pressure pulmonary edema	↑ Outside–inside pressure gradient	Laryngospasm
Acute lung injury and acute respiratory distress syndrome	↑ Permeability	Sepsis, aspiration, fat embolus, TRALI

TRALI, transfusion-related acute lung injury.

pH is more than 7.25, no intervention is necessary. If CO_2 retention is severe and the pH is less than 7.25 after increasing the respiratory rate to as high as 20 breaths per minute, administration of sodium bicarbonate should be considered.

To maximize oxygenation and limit exposure to potentially toxic concentrations of oxygen (i.e., $F_{IO_2} = 1$), usually an end-expiratory pressure of 10 cm H_2O is set.

In addition to standard monitoring, prolonged mechanical ventilation in ALI and ARDS will require arterial line placement to facilitate frequent arterial blood gas determinations. Further, a daily chest radiograph will be required.

The Acute Respiratory Distress Syndrome network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *N Engl J Med.* 2000;342:1301–1308.

D.6. If this patient had acute lung injury (ALI) secondary to aspiration, beside low-tidal volume ventilation, what other changes in routine therapy should be considered?

The newest "proven" management strategy noted to improve lung function and shorten the duration of mechanical ventilation and intensive care of patients with ALI is conservative administration of intravenous fluids. Although the protocol employed in the National Institutes of Health–sponsored study is too lengthy to expound on in this chapter, suffice it to say, the excessive administration of fluid is harmful, whereas minimizing intravenous fluids appears to be safe and not associated with other organ insufficiency or failure.

Wiedemann HP, Wheeler AP, Bernard GR, et al. National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network. Comparison of two fluid-management strategies in acute lung injury. *N Engl J Med.* 2006;354:2564–2575.

D.7. What therapies routinely administered by the anesthesiologist may cause ALI?

Transfusion-related acute lung injury has become the leading cause of transfusion-related morbidity and mortality in the United States. This injury is almost always recognized during or shortly after transfusion and is diagnosed by the absence of cardiac failure and fluid overload. Although any blood product can cause this injury, most recently, the transfusion of fresh frozen plasma and platelets, especially when donated by women who were previously pregnant, seem most responsible. This injury

can be seen even after the transfusion of a single blood product unit and "massive" transfusion is not, as previously thought, a prerequisite.

Triulzi DJ. Transfusion-related acute lung injury: current concepts for the clinician. *Anesth Analg.* 2009;108:770–776.

D.8. What methods of oxygen administration may be used postoperatively?

Most postoperative patients who are prone to develop hypoxemia may be managed with a nasal cannula or face mask. Nasal cannulas are cheap and comfortable, but regardless of flow rates, they cannot achieve an F_{IO_2} of more than 0.30. Face masks have the capability of delivering a wide range of precise F_{IO_2} levels of up to 1.

Occasionally, a patient may require more aggressive oxygen therapy than can be provided by nasal cannula or face mask, but less invasive than tracheal intubation and mechanical ventilation. Noninvasive positive pressure ventilation should be considered. Continuous positive airway pressure and bilevel positive airway pressure may be applied. These modes may be used in patients who either have previously used these devices at home or who are on the verge of requiring tracheal intubation and mechanical ventilation but have conditions thought to be rapidly resolving (e.g., CHF and chronic obstructive pulmonary disease exacerbation). These patients usually do not require an arterial catheter for blood sampling, but do need frequent assessment of their respiratory effort, particularly their respiratory rate and use of accessory muscles, as well as continuous Spo_2 monitoring. Several different types of masks are available. A respiratory therapist should be involved to individually achieve the best mask fit and patient comfort possible. Preparation to emergently tracheally intubate in case noninvasive ventilation fails must always be maintained.

Chanques JS, Jung B. Postoperative noninvasive ventilation. *Anesthesiology.* 2010;112: 453–461.

CHAPTER 59

Electroconvulsive Therapy

PATRICIA FOGARTY MACK

A 72-YEAR-OLD MAN

with major depressive disorder is scheduled for electroconvulsive therapy (ECT). His past medical history reveals significant coronary artery disease, status after three-vessel coronary bypass surgery 5 years ago. He also has chronic atrial fibrillation. He had a transient ischemic attack (TIA) 2 years previously after which he underwent left carotid endarterectomy. In addition, he has sleep apnea and gastroesophageal reflux disease (GERD). The patient weighs 115 kg and is 5 ft 3 in. tall and had a Mallampati class 2 airway. Medications include warfarin, atenolol, and esomeprazole (Nexium).

A. Medical Disease and Differential Diagnosis

1. What are the indications for ECT?
2. Are there any contraindications to ECT?
3. What is the mechanism of action of ECT?

B. Preoperative Evaluation and Preparation

1. How would you assess the cardiac status of this patient?
2. How should his anticoagulation be managed during ECT?
3. What implications do his history of sleep apnea have on management of ECT?
4. How does his history of TIA and carotid endarterectomy impact your preoperative evaluation?
5. Is ECT contraindicated in a patient with a permanent pacemaker or implantable cardiovertor-defibrillator?

C. Intraoperative Management

1. Describe the hemodynamic response to ECT in a typical patient.
2. Is an arterial line warranted in this patient?
3. By what means would you attempt to maximize hemodynamic stability?
4. Describe the cerebral hemodynamic effects of ECT.

5. How would you proceed with an anesthetic induction for this procedure?
6. How do you intend to manage his airway during each treatment?

D. Postoperative Management

1. The patient is extremely agitated upon emergence. Discuss the risk factors for postictal agitation (PIA) as well as the therapeutic options?
2. After three consecutive uneventful inpatient treatments, the psychiatrist asks if the patient may undergo ECT as an outpatient. Would you agree to this plan?

A. Medical Disease and Differential Diagnosis

A.1. What are the indications for ECT?

For centuries, it had been noted that psychosis did not tend to occur in those people with epilepsy. Since the 16th century, patients with severe mental illness were treated with various agents, such as camphor, to induce seizures (pharmacoconvulsive therapy). ECT was first instituted in the late 1930s and gained acceptance in providing a better-controlled seizure. The addition of curare, followed in 1951 by succinylcholine greatly diminished incidence of fracture due to the convulsions. Finally, the advent of methohexital, which ensured unconsciousness without significantly diminishing the seizure, led to the acceptance of ECT as an efficacious and safe treatment.

From the mid-1970s through the 1980s, many new drug treatments for psychiatric illness were developed and found to be efficacious. ECT fell into disfavor as a barbaric treatment when compared to pharmacotherapy.

In the past 15 years, the pendulum has again swung back in favor of ECT as a safe and effective treatment for drug-resistant major depressive disorder and bipolar disorder.

Specific indications for ECT include, but are not limited to major depressive disorder and bipolar disorder, nonchronic schizophrenia (especially with affective or catatonic symptoms) and schizoaffective disorder. Although usually reserved as a second-line therapy for those who are resistant to pharmacologic treatment, ECT has, in some circumstances, been recommended as a first-line therapy, especially if a rapid response is urgently required as in patients with severe suicidal potential, malnutrition/dehydration, and catatonia. Finally, ECT has been recommended in patients who are unable to tolerate pharmacotherapeutic agents for any reason, including during pregnancy.

American Psychiatric Association. *The Practice of Electroconvulsive Therapy: A Task Force Report of American Psychiatric Association*. 2nd ed. Washington, DC: American Psychiatric Association; 2001:5–26.

A.2. Are there any contraindications to ECT?

In the past, the only absolute contraindication was an intracranial mass lesion or vascular malformation; however, ECT has been performed successfully in patients with these diseases. There is considered to be significantly increased risk in patients with intracranial space occupying lesions, any condition associate with intracranial hypertension, recent myocardial infarction with diminished ventricular function, severe hypertension especially associated with pheochromocytoma, evolving stroke, retinal detachment, and any American Society of Anesthesiologists physical status 4 or 5 patient.

American Psychiatric Association. *The Practice of Electroconvulsive Therapy: A Task Force Report of American Psychiatric Association*. 2nd ed. Washington, DC: American Psychiatric Association; 2001:27–30.

Table 59.1	Mechanism of Action of Electroconvulsive Therapy—Physiological Theories
Neurophysiologic	
Anticonvulsant (changes in seizure threshold)	
Cerebral blood flow and metabolic rate changes	
Increased slow-wave EEG activity	
Antidelerium/sleep theories	
Neuroendocrinologic	
Prolactin release	
Neuropeptide release	
Melatonin	
Neurochemical	
Stimulation of β receptors	
Monoamine release	
Modulation of serotonin	

EEG, electroencephalography.

A.3. What is the mechanism of action of ECT?

The mechanism of ECT is unknown. There are many neurochemical, neuroendocrine, electrophysiologic, and neuropsychological theories regarding the mechanism of ECT. See Table 59.1.

In addition, although it has been long assumed that a generalized seizure of adequate duration is sufficient for effective treatment, recent research shows that barely suprathreshold stimulation, especially with unilateral ECT is not as efficacious. Current research suggests that something about the process of seizure generalization may be more important than the duration of the seizure.

B. Preoperative Evaluation and Preparation

B.1. How would you assess the cardiac status of this patient?

The cardiac status of the patient needs to be assessed as it would for any other general anesthetic. As there can be periods of significant tachycardia and hypertension following seizure induction, it would be useful to ensure that there is no longer significant myocardium at risk for ischemia and that systolic function is not compromised. If this information cannot be obtained from patient history and assessment of his functional status, it may be useful to obtain a stress test and echocardiogram. Bear in mind that it may be difficult to get an accurate history of functional status from patients who are psychotic or severely depressed.

American Psychiatric Association. *The Practice of Electroconvulsive Therapy: A Task Force Report of American Psychiatric Association*. 2nd ed. Washington, DC: American Psychiatric Association; 2001:77–80.

B.2. How should his anticoagulation be managed during ECT?

The anticoagulation for his atrial fibrillation should be continued throughout his course of therapy, maintaining an international normalized ratio (INR) between 2.0 and 3.0. Although intracerebral hemorrhage is a theoretic concern, a retrospective study from the Mayo Clinic suggests that ECT can be safely performed in patients on warfarin therapy.

American Psychiatric Association. *The Practice of Electroconvulsive Therapy: A Task Force Report of American Psychiatric Association*. 2nd ed. Washington, DC: American Psychiatric Association; 2001:40–41.

Mehta V, Mueller PS, Gonzalez-Arriaza HL, et al. Safety of electroconvulsive therapy in patients receiving long-term warfarin therapy. *Mayo Clin Proc*. 2004;79:1396–1401.

B.3. What implications do his history of sleep apnea have on management of ECT?

His history of sleep apnea is important because suboptimal management of respiratory function may reduce efficacy of treatment and increase complications. Hypocarbia is sometimes required to ensure adequate seizure duration. Additionally, after onset of seizure activity, oxygen consumption is increased dramatically as is CO_2 production. Hypercarbia can exacerbate the tachycardia and hypertensive responses to seizure. Therefore, adequate mask ventilation is required to ensure optimal respiratory status. The use of a laryngeal mask airway (LMA) may be required to ensure adequate ventilation in this patient.

Finally, if the patient uses continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BIPAP) at home, it may be useful to have that machine available to the patient in the postprocedure period when postanesthetic and postictal somnolence may compromise his ability to maintain a patent airway.

Saito S. Anesthesia management for electroconvulsive therapy: hemodynamic and respiratory management. *J Anesth*. 2005;19:142–149.

B.4. How does his history of TIA and carotid endarterectomy impact your preoperative evaluation?

A history of TIA or stroke, is an indication for computed tomography (CT) of the head before their first course of ECT. Another reason for patients to receive a head CT before initiation of ECT is to rule out an organic cause for depression. Although a comprehensive neurologic examination is routinely recommended by the American Psychiatric Association before ECT, it may be that in this patient, more sophisticated neuropsychological testing would be useful in documenting subtle deficits and establishing a true baseline. Finally, if the patient has not had follow-up carotid Doppler examination, it may be useful to ensure that there has not been restenosis or that no new plaques have formed. This is particularly important in view of the fact that the rate pressure product may be increased by as much as 400% in the sympathetic phase of the cardiac response.

American Psychiatric Association. *The Practice of Electroconvulsive Therapy: A Task Force Report of American Psychiatric Association*. 2nd ed. Washington, DC: American Psychiatric Association; 2001:77–80.

B.5. Is ECT contraindicated in a patient with a permanent pacemaker or implantable cardiovertor-defibrillator?

See Chapter 7, section C.11.

C. Intraoperative Management

C.1. Describe the hemodynamic response to ECT in a typical patient.

First, a parasympathetic discharge occurs within a few seconds of application of the electrical stimulus. This may result in bradycardia, which may be profound and even progress to asystole. Because many patients are volume depleted due to poor oral intake or mildly hypotensive secondary to their psychotropic medications, they can be susceptible to further hypotension due to anesthetic induction. Within 1 minute, sympathetic activation due to the seizure results in a tachycardia and at times dysrhythmias as well as hypertension to up to 150% of baseline values. This hypertension usually lasts for between 2 and 5 minutes. If the patient is not adequately ventilated, hypercarbia may add to the hypertension. During the first ECT treatment, the electrical stimulus may often be titrated upward in succession until a generalized seizure occurs. When a generalized seizure does not follow the electrical stimulation, the parasympathetic response predominates and the patient may experience a sustained bradycardia.

With such a dramatic increase in heart rate and blood pressure, the rate pressure product, an indicator of myocardial oxygen demand, is significantly elevated. This can lead to electrocardiographic ischemia as well as regional wall motion abnormalities on echocardiography.

Messina AG, Paranicas M, Katz B, et al. Effect of electroconvulsive therapy on the electrocardiogram and the echocardiogram. *Anesth Analg.* 1992;75:511–514.

Saito S. Anesthesia management for electroconvulsive therapy: hemodynamic and respiratory management. *J Anesth.* 2005;19:142–149.

C.2. Is an arterial line warranted in this patient?

No, in spite of the potential dramatic perturbations in heart rate and blood pressure, these responses are fairy predictable and can be attenuated by judicious use of anticholinergics and antihypertensives. Atropine (0.4 mg) or glycopyrrolate (0.2 mg) are used to prevent the bradycardia associated with the parasympathetic discharge. The tachycardia and hypertension seen as part of the sympathetic response can be prevented with short acting β-blockade, nitroglycerin, or even remifentanil, administered just at the beginning of the sympathetic stimulation.

Severe cardiac complications during ECT are very rare.

Saito S. Anesthesia management for electroconvulsive therapy: hemodynamic and respiratory management. *J Anesth.* 2005;19:142–149.

C.3. By what means would you attempt to maximize hemodynamic stability?

First, one should continue antihypertensive medication on the evening before and the morning of the procedure. Second, a small dose of atropine (0.4 mg) or glycopyrrolate (0.2 mg) may be given several minutes before the electrical stimulation in order to prevent the subsequent bradycardia. At Weill Cornell Medical Center, we

are more likely to use glycopyrrolate as it is a quaternary compound, which will not cross an intact blood–brain barrier. In addition, the tachycardic response from the seizure is not as pronounced when glycopyrrolate is used as compared with atropine. Anticholinergic pretreatment is most important during the first treatment when the electrical stimulation is being titrated and it is likely not to progress into a generalized seizure on the first or second stimulus. If the pretreatment with an anticholinergic leaves a fragile patient with an undesirable tachycardia, we may omit it during subsequent treatments as long as the bradycardia is not too severe or prolonged.

Similarly, medications to attenuate the sympathetic response are typically not administered until it is certain that the seizure will generalize. This results in a requirement for very fast-acting drugs to control heart rate and blood pressure. The drug of choice at Weill Cornell Medical Center is esmolol (0.5 to 1.0 mg per kg) or labetalol (5 to 20 mg). If there is a contraindication to β-blockers, diltiazem, nicardipine, or sodium nitroprusside may be substituted. Nitroglycerin may be particularly useful in patients with ischemic cardiac disease. Remifentanil has also been found to be effective in attenuating the sympathetic response.

A recent study of American Society of Anesthesiologists I and II patients assessed echocardiographic and hemodynamic parameters when the sympathetic response was pretreated with β–blocker, calcium channel blocker, or nitroglycerin prior to the electrical stimulus. No new regional wall motion abnormalities were found, but β–blocker seemed to be the most effective medication at attenuating fractional shortening and the entire sympathetic response.

Kadoi Y, Saito S, Takahashi K-I, et al. Effects of antihypertensive medication on left ventricular function during electroconvulsive therapy: study with transthoracic echocardiography. *J Clin Anesth*. 2006;18:441–445.

Saito S. Anesthesia management for electroconvulsive therapy: hemodynamic and respiratory management. *J Anesth*. 2005;19:142–149.

Van Zijl DH, Gordon PC, James MF. The comparative effects of remifentanil or magnesium sulfate versus placebo on attenuating the hemodynamic responses after electroconvulsive therapy. *Anesth Analg*. 2005;101:1651–1655.

C.4. Describe the cerebral hemodynamic effects of ECT.

Electrically induced seizures lead to cerebral hyperemia (increase in cerebral blood flow) as documented by transcranial Doppler and near-infrared spectroscopy. This response occurs even if the seizure does not generalize, suggesting that they are a result of the electric stimulation itself. The increase in cerebral blood flow has been shown to be related to the degree of systemic hypertension and occurs whether bilateral or unilateral stimulus is applied. Although there is a correlation with systemic hypertension, the systemic antihypertensives do not fully ameliorate the increase in cerebral blood flow. This is due to the fact that these drugs have differing effects on the cerebral and systemic circulations.

Saito S. Anesthesia management for electroconvulsive therapy: hemodynamic and respiratory management. *J Anesth*. 2005;19:142–149.

C.5. How would you proceed with an anesthetic induction for this procedure?

Anesthetic induction may be accomplished with any one of a number of medications. Traditionally methohexital (0.5 to 1.0 mg per kg) has been the induction agent of choice because it has very little effect on seizure duration and has a rapid onset and recovery profile. Unfortunately, methohexital is no longer available in

many areas. At Weill Cornell Medical Center, we now use etomidate (0.2 to 0.3 mg per kg). In research studies, etomidate provides for longer seizure duration when compared to methohexital and propofol; however, postictal hypertension is more severe and myoclonic contractions may be undesirable. In addition, there is a greater incidence of nausea, increased confusion, and prolonged recovery time. Although adrenal suppression has been reported in patients on continuous infusions of etomidate, there are no reports of adrenal suppression in patients receiving multiple bolus doses of etomidate as part of a course of ECT. In patients in whom etomidate is not well tolerated, propofol or thiopental may be used. Studies concur that propofol and thiopental reduce seizure duration; however, there is controversy as to how this reduction in seizure duration impacts the efficacy of therapy.

Ketamine has been noted to have antidepressant effects and potentiate the early reduction of depressive symptoms when given in conjunction with ECT. It appears that ketamine may be useful in some patients in whom a rapid decrease in depressive symptoms is essential, such as those with extreme suicidal ideation or catatonia. Randomized trials addressing the potential long-term benefits and disadvantages versus other induction agents are warranted.

Muscle relaxation is usually achieved with succinylcholine (0.5 to 1.0 mg per kg) unless there is a contraindication. In that case, an appropriate nondepolarizing muscle relaxant may be substituted.

Ding Z, White PF. Anesthesia for electroconvulsive therapy. *Anesth Analg*. 2002;94: 1351–1364.

Okamoto N, Nakai T, Sakamoto K, et al. Rapid antidepressant effect of ketamine anesthesia during electroconvulsive therapy of treatment-resistant depression: comparing ketamine and propofol anesthesia. *J ECT*. 2010;26:223–227.

Saito S. Anesthesia management for electroconvulsive therapy: hemodynamic and respiratory management. *J Anesth*. 2005;19:142–149.

C.6. How do you intend to manage his airway during each treatment?

The diagnosis of sleep apnea and the patient's body habitus raise concerns regarding the ease and effectiveness of mask ventilation. In spite of these concerns, I would proceed with a plan for mask ventilation with a backup plan of LMA or intubation. As ECT is usually administered three times a week, repeated intubations may lead to airway trauma and edema. GERD may also be of concern; however, we do not intubate patients for ECT solely because of GERD. Our plan would include continuation of medication to reduce stomach acid and promote gastric emptying, as well as a dose of preinduction sodium bicitrate.

Effective mask ventilation is important for several reasons. First, hypocapnea may lower seizure threshold and promote more effective therapy. Second, avoidance of hypercapnea postseizure is necessary as hypercapnea will exacerbate hypertension and tachycardia.

In anticipation of potential difficult ventilation during ECT, we proceed with oxygenation for 3 to 5 minutes prior to induction. As soon as induction is accomplished, both an oral and a well-lubricated nasal airway will be placed. A second person ideally is available in case two-person ventilation is required. We find that Jackson-Reese circuits are advantageous for ventilation during ECT. First, they allow you to adjust the amount of positive pressure administered; second, the weight of an Ambu bag can sometimes make maintenance of ideal mask placement difficult; finally, as the patient regains spontaneous ventilation, he or she may breathe comfortably and effectively through the Jackson-Reese circuit. If mask ventilation were not effective, I would place an appropriately sized LMA.

If necessary for adequate ventilation, intubation may be considered. Unfortunately, repeated intubations over several days and weeks may lead to glottic edema and trauma.

Saito S. Anesthesia management for electroconvulsive therapy: hemodynamic and respiratory management. *J Anesth.* 2005;19:142–149.

D. Postoperative Management

D.1. The patient is extremely agitated upon emergence. Discuss the risk factors for postictal agitation (PIA) as well as the therapeutic options?

PIA manifests as disorientation, inability to consistently follow commands, and motor agitation. Risk factors for PIA include prolonged seizure duration, bilateral versus unilateral ECT, and concomitant lithium therapy. In addition, low doses of induction agent as well as very low doses of succinylcholine are considered risk factors. The etiology of low-dose succinylcholine may be related to excess lactate production in those patients who have greater manifestation of clinical seizure activity. Increased lactate levels were noted in patients who experienced PIA versus those who did not.

It is of critical importance to rule out nonconvulsive status epilepticus as an etiology for the PIA. Nonconvulsive status may present as agitation or conversely as mutism.

Treatment of PIA usually consists of benzodiazepine, such as midazolam 1 to 2 mg. If this is not effective, haloperidol may be added. In some circumstances, propofol as a bolus or an infusion have been effective.

Augoustides JG, Greenblatt E, Abbas MA, et al. Clinical approach to agitation after electroconvulsive therapy: a case report and literature review. *J ECT*. 2002;18: 213–217.

D.2. After three consecutive uneventful inpatient treatments, the psychiatrist asks if the patient may undergo ECT as an outpatient. Would you agree to this plan?

Outpatient ECT has become an acceptable therapeutic option in our institution for many patients. Primarily, it is used for maintenance therapy. It may also be used to complete an initial course of ECT provided that the first several treatments are uneventful medically (i.e., no respiratory or cardiovascular problems) and that the patient is demonstrating improvement in psychiatric status. In addition, because psychiatric patients may be unreliable in following preoperative instructions, such as nothing by mouth status, they must have another adult who assumes responsibility for ensuring that those instructions are followed. Of course, they must also have an escort to bring them home.

Finally, there needs to be close communication between the treating psychiatrist and the ECT psychiatrist to keep abreast of any change in psychiatric status or in any medical condition.

CHAPTER 60

Ambulatory Surgery

KATHRYN E. MCGOLDRICK

A 38-YEAR-OLD WOMAN desiring permanent sterility was scheduled for bilateral laparoscopic tubal ligation in the ambulatory surgical suite. Her preoperative outpatient questionnaire indicated a history of glaucoma. Additionally, she had surgery 2 weeks ago under general anesthesia for a detached retina, and her postoperative course was complicated by severe postoperative nausea and vomiting (PONV). She is 5 ft 7 in. tall, weighs 195 lbs, and complains of chronic fatigue. Her only medications consist of "eye drops."

A. Pathophysiology and Differential Diagnosis

1. What are the anesthetic implications of glaucoma?
2. What side effects and important anesthetic interactions are associated with eye drops used to treat glaucoma?
3. Should glaucoma medications be discontinued before elective surgery?
4. Is this patient morbidly obese?
5. What medical conditions may be associated with obesity and morbid obesity?

B. Preoperative Evaluation and Preparation

1. What advantages does outpatient surgery offer?
2. What are the goals of the preoperative evaluation of the surgical outpatient?
3. In order to thoroughly screen for disease, should one put all outpatients through a full battery of laboratory testing?
4. What preoperative laboratory testing is necessary for the surgical outpatient?
5. Which outpatients should receive a preoperative chest radiograph?
6. In which patients is an electrocardiogram (ECG) necessary before outpatient anesthesia and surgery?
7. Would a patient's age or physical status influence the decision to perform outpatient surgery?

8. What patients would be considered inappropriate for ambulatory surgery?
9. What questions are critically important to ask this patient when obtaining her medical history?
10. How would you premedicate this patient?
11. Should every outpatient receive prophylaxis against acid aspiration pneumonitis?
12. Is an overnight fast justified for all outpatients?

C. Intraoperative Management

1. What are the important considerations in choosing an anesthetic technique for outpatient surgery?
2. What are the anesthetic implications of recent retinal detachment surgery?
3. How would you monitor this patient?
4. What is the Bispectral Index (BIS) monitor and what information does it convey?
5. What benefits might be derived from using a BIS monitor?
6. Is BIS monitoring applicable to children?
7. What are the major limitations of BIS monitoring?
8. What does a BIS reading of 56 mean?
9. What are the anesthetic options for laparoscopy?
10. Under what circumstances might spinal anesthesia be appropriate for outpatient laparoscopy?
11. What anesthetic agents would you use to induce and maintain general anesthesia in this patient?
12. Would you avoid the use of nitrous oxide in this ambulatory patient?
13. Discuss the physiologic changes induced by laparoscopy.
14. In addition to the physiologic changes described in the preceding text, what other intraoperative complications are associated with laparoscopy?
15. Why is carbon dioxide the insufflation agent of choice for laparoscopy?
16. What are some alternatives to carbon dioxide for laparoscopy?

D. Postoperative Management

1. What are the common causes of nausea and vomiting in outpatients?
2. How would you pharmacologically prevent PONV in the susceptible ambulatory patient?
3. How is postoperative pain treated?
4. If the patient complained of eye pain postoperatively, how would you manage the situation?
5. What criteria would you use to establish that a patient can be safely discharged after ambulatory surgery?
6. How would you decide when to discharge a patient after regional anesthesia?
7. What instructions should be given to an ambulatory surgical patient upon discharge?

A. Pathophysiology and Differential Diagnosis

A.1. What are the anesthetic implications of glaucoma?

With open-angle glaucoma, elevated intraocular pressure (IOP) exists in conjunction with an anatomically patent anterior chamber angle. It is thought that sclerosis of trabecular tissue produces impaired aqueous filtration and drainage. Treatment consists of medication to produce miosis and trabecular stretching. Commonly used eye

drops include epinephrine, echothiophate iodide, timolol, dipivefrin, and betaxolol. Carbonic anhydrase inhibitors such as acetazolamide can also be administered by various routes to reduce IOP by interfering with the production of aqueous humor. All these drugs are systemically absorbed and can, therefore, have anticipated side effects.

It is important to appreciate that maintenance of IOP is determined primarily by the rate of aqueous formation and the rate of aqueous outflow. The most important influence on formation of aqueous humor is the difference in osmotic pressure between aqueous humor and plasma. This concept is illustrated by the equation:

$$IOP = K\,[(OP_{aq} - OP_{pl}) + CP]$$

where K = coefficient of outflow, OP_{aq} = osmotic pressure of aqueous humor, OP_{pl} = osmotic pressure of plasma, and CP = capillary pressure. The fact that a small change in solute concentration of plasma can dramatically affect the formation of aqueous humor and hence IOP is the rationale for administering hypertonic solutions, such as mannitol, to reduce IOP. Fluctuations in aqueous outflow can also markedly change IOP. The primary factor controlling aqueous humor outflow is the diameter of Fontana's spaces, as illustrated by the equation:

$$A = \frac{r^4 \times (P_{IOP} - P_v)}{8\eta L}$$

where A = volume of aqueous outflow per unit of time, r = radius of Fontana's spaces, P_{IOP} = IOP, P_v = venous pressure, η = viscosity, and L = length of Fontana's spaces. When the pupil dilates, Fontana's spaces narrow, resistance to outflow is increased, and IOP rises. Because mydriasis is undesirable in both closed- and open-angle glaucoma, miotics such as pilocarpine are applied conjunctivally in patients with glaucoma to effect papillary constriction.

The aforementioned equation describing the volume of aqueous outflow per unit of time clearly underscores that outflow is exquisitely sensitive to fluctuations in venous pressure. Because an elevation in venous pressure results in an increased volume of ocular blood as well as decreased aqueous outflow, it is obvious that a considerable increase in IOP occurs with any maneuver that increases venous pressure. Hence, in addition to preoperative instillation of miotics, other anesthetic objectives for the patient with glaucoma include perioperative avoidance of venous congestion and of overhydration. Furthermore, hypotensive episodes are to be avoided because these patients are purportedly vulnerable to retinal vascular thrombosis.

Although glaucoma usually occurs as an isolated disease, it may also be associated with such conditions as Sturge-Weber syndrome, aniridia, mesodermal dysgenesis syndrome, retinopathy of prematurity, Refsum syndrome, mucopolysaccharidosis, Hurler syndrome, Stickler syndrome, Marfan syndrome, and von Reckinghausen disease (neurofibromatosis). Additionally, ocular trauma, steroid therapy, sarcoidosis, some forms of arthritis associated with uveitis, and pseudoexfoliation syndrome can also be associated with secondary glaucoma.

Primary closed-angle glaucoma is characterized by a shallow anterior chamber and a narrow iridocorneal angle that impedes the egress of aqueous humor from the eye because the trabecular meshwork is covered by the iris. Relative pupillary block is common in many angle-closure episodes in which iris–lens apposition or synechiae impede the flow of aqueous from the posterior chamber. In the United States, the prevalence of angle-closure glaucoma (ACG) is one-tenth as common as open-angle glaucoma. In acute ACG, if the pressure is not reduced promptly, permanent visual loss can ensue as a result of optic nerve damage. It is thought that irreversible optic nerve injury can occur within 24 to 48 hours.

McGoldrick KE. Eye, ear, nose, and throat diseases. In: Fleisher LA, ed. *Anesthesia and Uncommon Diseases*. 5th ed. Philadelphia: WB Saunders; 2006:4–5.

McGoldrick KE, Gayer SI. Anesthesia for ophthalmologic surgery. In: Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1321–1345.

A.2. What side effects and important anesthetic interactions are associated with eye drops used to treat glaucoma?

Echothiophate is a long-acting anticholinesterase miotic that lowers IOP by decreasing resistance to the outflow of aqueous humor. Useful in the treatment of glaucoma, echothiophate is absorbed into the systemic circulation after instillation in the conjunctival sac. Any of the long-acting anticholinesterases may prolong the action of succinylcholine because, after a month or more of therapy, plasma pseudocholinesterase activity may be less than 5% of normal. It is said, moreover, that normal enzyme activity does not return until 4 to 6 weeks after discontinuation of the drug. Hence, the anesthesiologist should anticipate prolonged apnea if these patients are given a customary dose of succinylcholine. In addition, a delay in metabolism of ester local anesthetics should be expected.

Although topical epinephrine has proved useful in some patients with open-angle glaucoma, the 2% solution has been associated with such systemic effects as nervousness, hypertension, angina pectoris, tachycardia, and other dysrhythmias.

Timolol, a nonselective β-adrenergic blocking drug, has historically been a popular antiglaucoma drug. Because significant conjunctival absorption may occur, timolol should be administered with caution to patients with known obstructive airway disease, severe congestive heart failure, or greater than first-degree heart block. Life-threatening asthmatic crises have been reported after the administration of timolol drops to some patients with chronic, stable asthma. Not unexpectedly, the development of severe sinus bradycardia in a patient with cardiac conduction defects (left anterior hemiblock, first-degree atrioventricular block, and incomplete right bundle-branch block) has been reported after timolol. Moreover, timolol has been implicated in the exacerbation of myasthenia gravis and in the production of postoperative apnea in neonates and young infants. Patients may report feelings of fatigue and/or depression in association with the use of timolol drops.

In contrast to timolol, a newer antiglaucoma drug, betaxolol, a β_1-blocker, is said to be more oculospecific and have minimal systemic effects. However, patients receiving an oral β-blocker and betaxolol should be observed for potential additive effects on known systemic effects of β-blockade. Caution should be exercised in patients receiving catecholamine-depleting drugs. Although betaxolol has produced only minimal effects in patients with obstructive airway disease, caution should be exercised in the treatment of patients with excessive restriction of pulmonary function. Moreover, betaxolol is contraindicated in patients with sinus bradycardia, greater than first-degree heart block, cardiogenic shock, and overt myocardial failure.

McGoldrick KE, Gayer SI. Anesthesia for ophthalmologic surgery. In: Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1321–1345.

A.3. Should glaucoma medications be discontinued before elective surgery?

For all the aforementioned reasons, it is important to continue glaucoma medications in the perioperative period. Moreoever, the anesthesiologist must be aware of

which medications the patient is taking and the effects of these drugs on anesthetic management.

McGoldrick KE, Gayer SI. Anesthesia for ophthalmologic surgery. In: Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1321–1345.

A.4. Is this patient morbidly obese?

Morbid obesity is defined by a body mass index greater than 40 kg per m^2. This patient has a body mass index of approximately 30 and would, therefore, be considered obese. See Chapter 62, section A.2.

Ogunnnaike BO, Whitten CW. Anesthesia and obesity. In: Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1230–1246.

A.5. What medical conditions may be associated with obesity and morbid obesity?

A plethora of conditions may be associated with obesity and morbid obesity including diabetes, hyperlipidemia, cholelithiasis, gastroesophageal reflux disease, cirrhosis, degenerative joint and disk disease, venous stasis and thrombotic/embolic disease, sleep disorders including obstructive sleep apnea, several types of cancer, and emotional disorders. Diseases of the cardiopulmonary system are common and concerning. They include, but are not limited to, systemic hypertension, pulmonary hypertension and cor pulmonale, restrictive lung disease, and right and left ventricular hypertrophy.

Neligan PJ, Porter S, Max B, et al. Obstructive sleep apnea is not a risk factor for difficult intubation in morbidly obese patients. *Anesth Analg*. 2009;109:1181–1186.

Qadir N, Smith I. Day surgery: how far can we go and are there still limits? *Curr Opin Anaesthesiol*. 2007;20:503–507.

B. Preoperative Evaluation and Preparation

B.1. What advantages does outpatient surgery offer?

Outpatient surgery typically offers greater convenience to the patient (less time away from home, family, and work), a more pleasant environment with less stress and emotional disturbance, and a reduced risk of infection, particularly for the immunocompromised or the pediatric patient. Additionally, outpatient surgery is more economical and enables more efficient use of operating rooms with greater flexibility in scheduling surgery. Finally, one is not dependent on the availability of hospital beds.

Lichtor JL. Ambulatory anesthesia. In: Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:833–846.

B.2. What are the goals of the preoperative evaluation of the surgical outpatient?

The objectives of the preoperative evaluation are as follows:

- To perform medical assessments, obtain data, arrange for laboratory tests and consultations as indicated, and prescreen for relevant conditions in order to optimize perioperative outcome
- To obtain informed consent
- To provide information and instructions to reduce patient anxiety and improve perioperative management

Organization of the preoperative screening varies among ambulatory surgical facilities throughout the country. The screening process may be organized with an office or facility visit before the day of surgery, by a telephone interview or review of health questionnaire without a visit, or by preoperative screening and visit on the morning of surgery. Each of these systems has its advantages and disadvantages. Nevertheless, the system for preoperative evaluation of ambulatory surgical patients should ensure that screening is performed far enough in advance so that pre-existing disease can be evaluated, treatment optimized, and laboratory data recorded before the patient presents for anesthesia. Written instructions should be supplied to the patient in advance describing the preoperative workup, admission, and recovery periods.

Hata TM, Moyers JR. Preoperative patient assessment and management. In: Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:569–597.

Lichtor JL. Ambulatory anesthesia. In: Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:833–846.

B.3. In order to thoroughly screen for disease, should one put all outpatients through a full battery of laboratory testing?

No. The practice of preoperative "shotgun" laboratory screening for outpatient surgery has received much criticism. In addition to unnecessarily adding several billion dollars annually to the cost of healthcare, laboratory screening tests in asymptomatic patients have been shown to be of dubious value. History and physical examination are a better means of screening for disease and should serve to reduce expensive, potentially harmful, and inappropriate tests.

Chung F, Yuan H, Yin L, et al. Elimination of preoperative testing in ambulatory surgery. *Anesth Analg*. 2009;108:467–475.

Hata TM, Moyers JR. Preoperative patient assessment and management. In: Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:569–597.

Pasternak LR. Does reoutine testing affect outcome? In: Fleisher LA, ed. *Evidence-Based Practice of Anesthesiology*. 2nd ed. Philadelphia: Saunders Elsevier; 2009:11–14.

B.4. What preoperative laboratory testing is necessary for the surgical outpatient?

Most outpatient surgical facilities consider the operative procedure and the patient's age, medical condition, medication history, and state and local regulations in determining which preoperative tests are "required." For the healthy ambulatory patient

between the ages of 1 and 40 years having a minor surgical procedure, no laboratory testing may be required. Pregnancy testing is a highly controversial issue. Many believe that pregnancy testing should be offered to all consenting females of childbearing potential. This approach, however, does not substitute for an appropriate pregnancy history and physical examination. Hemoglobin or hematocrit determination is appropriate for surgical procedures associated with substantial blood loss (unlikely in the ambulatory venue), and for patients at risk for anemia or polycythemia, such as children younger than 1 year or with suspected sickle cell disease, patients with a history of anemia, blood dyscrasia or malignancy, patients with congenital heart disease or chronic disease, women with heavy menstrual flow, and patients older than 60 years old. Additional testing depends on an individual's pre-existing condition. For example, serum electrolyte testing would be indicated for a patient with a history of hypertension, diabetes mellitus, renal disease, or for those patients taking diuretics, digoxin, steroids, or angiotension-converting enzyme inhibitors. Likewise, measurement of the partial thromboplastin time and the prothrombin time would be indicated in the presence of a bleeding disorder, anticoagulant use, liver disease, or poor nutritional status. Preoperative urinalysis has not been shown to be useful as a screening test, and is no longer required in a routine anesthetic evaluation.

Finnegan BA, Rashiq S, McAlister FA, et al. Selective ordering of preoperative investigations by anesthesiologists reduces the number and cost of tests. *Can J Anaesth*. 2005;52:575–580.

Narr BJ, Brown DR. Should preoperative hemoglobin always be obtained? In: Fleisher LA, ed. *Evidence-Based Practice of Anesthesiology*. 2nd ed. Philadelphia: Saunders Elsevier; 2009:24–27.

Steffey CS, Twersky RS. Is routine preoperative pregnancy testing necessary? In: Fleisher LA, ed. *Evidence-Based Practice of Anesthesiology*. 2nd ed. Philadelphia: Saunders Elsevier; 2009:28–32.

B.5. Which outpatients should receive a preoperative chest radiograph?

Abnormalities in the chest radiograph in asymptomatic patients are rare, and the risks to the patient probably exceed the benefits. A preoperative chest x-ray is indicated only for patients with a history or clinical findings of active pulmonary disease. Extremes of age, smoking, stable chronic obstructive pulmonary disease, stable cardiac disease, or resolved recent upper respiratory infection should not be considered absolute indications for chest x-ray.

American Society of Anesthesiologists Task Force on Preanesthesia Evaluation. Practice advisory for preanesthesia evaluation: a report by the American Society of Anesthesiologists task force on preanesthesia evaluation. *Anesthesiology*. 2002;96: 485–466; amended on page 492 by the ASA House of Delegates on October 15, 2003.

Joo HS, Wong J, Naik VN, et al. The value of screening preoperative chest x-rays: a systematic review. *Can J Anaesth*. 2005;52:568–574.

B.6. In which patients is an electrocardiogram (ECG) necessary before outpatient anesthesia and surgery?

It has not been established that information obtained from the preoperative ECG affects clinical care. Indeed, the American College of Cardiology/American Heart Association (ACC/AHA) guidelines published in 2007 are silent on the need for a preoperative ECG based on age alone. Nonetheless, Correll and colleagues found that age >65 years is an independent predictor of preoperative ECG abnormalities. The ACC/

AHA guidelines consider ambulatory surgery as one entity, classifying *all* ambulatory procedures as low risk, with reported cardiac mortality <1%. These guidelines reflect the belief that in the absence of active cardiac conditions (defined as unstable coronary syndromes, decompensated heart failure, significant arrhythmias [e.g., high-degree atrioventricular block, symptomatic ventricular arrhythmias, and supraventricular tachycardia with uncontrolled ventricular rate]), cardiovascular testing in stable patients would rarely result in a change in management and it would be a appropriate to proceed with surgery.

In general, a preoperative ECG should be considered in ambulatory patients in whom there is a reasonably high likelihood of cardiac dysfunction and the results of the ECG would have the potential to influence perioperative management. Clearly, the patient's history—including a thorough exploration of activity level and exercise tolerance—the physical examination, and the proposed surgical procedure are vital elements in the assessment of whether an ECG is indicated.

Correll DJ, Hepner DL, Chang C, et al. Preoperative electrocardiograms: patient risk factors predictive of abnormalities. *Anesthesiology*. 2009;110:1217–1222.

Fleisher LA, Beckman JA, Brown KA, et al. ACC/AHA 2007 Guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery. *Circulation*. 2007;116:1971–1996.

Gold BS. Who should have a preoperative 12-lead electrocardiogram? In: Fleisher LA, ed. *Evidence-Based Practice of Anesthesiology*. 2nd ed. Philadelphia: Saunders Elsevier; 2009:20–23.

B.7. Would a patient's age or physical status influence the decision to perform outpatient surgery?

Even patients at the extremes of age (e.g., younger than 6 months and older than 80 years) have been managed successfully at ambulatory centers throughout the country. With the exception of the former preterm infant and newborns in the first few weeks of life, age alone should not be considered a deterrent in the selection of patients for outpatient surgery. Premature infants (gestational age at birth <37 weeks) who undergo general anesthesia during the first months of life are at increased risk for postoperative apnea for up to 12 hours. This risk is greatest for infants younger than 46 weeks postconceptional age, but some investigators have reported apnea in infants as old as 60 weeks postconceptional age. Unfortunately, the postconceptional age at which the former premature infant no longer represents an increased risk for postoperative apnea, and therefore, would be considered an acceptable candidate for an ambulatory surgical procedure is not absolutely known. Therefore, at the present time, it is safest to admit to a hospital or to a 24-hour recovery unit all former premature infants less than 46 weeks postconceptional age so that they can be monitored for apnea. Many anesthesiologists are more conservative and adhere to cut-offs ranging from 52 to 60 weeks postconceptional age. If anemia, bronchopulmonary dysplasia, or other neonatal problems are present, this period may need to be extended. Likewise, postoperative apneic episodes have been described in otherwise healthy full-term infants who are anesthetized in the first few weeks of life. For this reason, many anesthesiologists are reluctant to proceed with outpatient anesthesia and surgery on a healthy full-term infant of less than 2 to 4 weeks of age.

For the geriatric patient, recent clinical experience has not demonstrated an age-related effect on the duration of recovery or the incidence of postoperative complications after outpatient surgery. However, in determining the acceptability of a geriatric patient for an ambulatory surgical procedure, one must consider the patient's physiologic age and physical status, the surgical procedure, the anesthetic technique, and the quality of care that will be provided at home. Chronologic age per se is not a determinant of suitability for ambulatory surgery.

No longer is outpatient surgery restricted to patients of American Society of Anesthesiologists (ASA) physical status I and II. ASA physical status III and IV patients whose diseases are well controlled preoperatively may be considered acceptable candidates for outpatient surgery.

Cravero JP, Kain ZN. Pediatric anesthesia. In: Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1206–1220.

McGoldrick KE. Anesthesia considerations for the geriatric outpatient. In: Silverstein JH, Rooke GA, Reeves JC, et al., eds. *Geriatric Anesthesiology*. 2nd ed. New York: Springer; 2008:322–337.

B.8. What patients would be considered inappropriate for ambulatory surgery?

An individual may be classified as an inappropriate ambulatory surgery patient for the following reasons:

- The existence of a condition that places an infant at risk
- History of prematurity in an infant less than 46 to 60 weeks postconceptional age
- Apneic episodes, feeding difficulty, or failure to thrive
- Respiratory distress syndrome that has required intubation and ventilatory support (may take up to a year for symptoms to resolve)
- Bronchopulmonary dysplasia with any degree of significant decrease in pulmonary function or requirement for supplemental oxygen
- Acute concurrent illness
- ASA physical status III or IV with poorly controlled disease
- Active cardiac conditions, as defined by ACC/AHA Guidelines
- Acute substance abuse
- Morbid obesity with other serious systemic diseases, such as severe obstructive sleep apnea and ventricular dysfunction
- Placement of a bare metal stent within 4 to 6 weeks of the proposed surgery
- Placement of a drug-eluting stent less than at least 1 year before the date of proposed surgery
- No available adult at home
- Refusal to have surgical procedure done as an outpatient
- Unwilling to follow instructions

The appropriateness of each patient must be evaluated on an individual basis, taking into account a combination of several factors, such as the patient's circumstances, the nature of the surgical procedure, anesthetic technique, anticipated severity of postoperative pain, and comfort level of the anesthesiologist.

Augoustides JGT, Riha H, Fleisher LA. How long should you wait after percutaneous coronary intervention for noncardiac surgery? In: Fleisher LA, ed. *Evidence-Based Practice of Anesthesiology*. 2nd ed. Philadelphia: Saunders Elsevier; 2009:79–86.

Cravero JP, Kain ZN. Pediatric anesthesia. In: Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1206–1220.

Fleisher LA, Beckman JA, Brown KA, et al. ACC/AHA 2007 Guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery. *Circulation*. 2007;116:1971–1996.

Lichtor JL. Ambulatory anesthesia. In: Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:833–846.

McGoldrick KE. Anesthesia considerations for the geriatric outpatient. In: Silverstein JH, Rooke GA, Reeves JC, et al., eds. *Geriatric Anesthesiology*. 2nd ed. New York: Springer; 2008:322–337.

Practice alert for the perioperative management of patients with coronary artery stents. A report by the American Society of Anesthesiologists Committee on Standards and Practice Parameters. *Anesthesiology*. 2009;110:22–23.

B.9. What questions are critically important to ask this patient when obtaining her medical history?

It is important to acquire as much information as possible about the patient's eye disease. For example, does she have open- or closed-angle glaucoma? What eye drops is she taking? When she had retinal detachment surgery 2 weeks ago, did the ophthalmic surgeon inject an air or gas bubble to tamponade the retina? If so, which substance was injected and has it been fully resorbed? Additionally, it is important to rule out obstructive sleep apnea in view of the patient's obesity and her complaints of fatigue. Does she snore, have frequent awakenings during the night, and does she fall asleep commonly during the daytime? Obese patients with severe sleep apnea and certain associated conditions (pulmonary hypertension, ventricular dysfunction, etc.) having painful surgery under general anesthesia that may require significant amounts of opioids postoperatively for pain control are typically considered poor candidates for planned outpatient surgery.

American Society of Anesthesiologists Task Force on Perioperative Management. *Practice Guidelines for the Perioperative Management of Patients with Obstructive Sleep Apnea. A Report by the American Society of Anesthesiologists Task Force on Management of Patients with Obstructive Sleep Apnea*. Approved by the House of Delegates on October 25, 2005.

McGoldrick KE, Gayer SI. Anesthesia for ophthalmologic surgery. In: Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1321–1345.

B.10. How would you premedicate this patient?

Whether the ambulatory surgical patient should receive premedication has been the subject of much interest and debate. Keeping in mind that a prompt recovery is an important consideration in outpatient anesthesia, many authors have recommended that little or no premedication (especially the centrally active depressant premedicants) be given to surgical outpatients so that recovery is not prolonged. Interestingly, most prospective clinical studies have failed to demonstrate a prolonged recovery following premedication with sedative-anxiolytic and analgesic drugs. However, narcotic premedicants have been shown to increase the incidence of postoperative nausea, which could prolong recovery time, and are not recommended unless the patient is in pain preoperatively.

In view of the goals one might want to achieve with outpatient preoperative medication, including anxiety relief, sedation, amnesia, analgesia, vagolysis, prophylaxis against aspiration pneumonia, and prevention of PONV premedicant drugs may be safely used if needed by the patient, provided the drug and the dosage are carefully chosen. Drugs commonly used as premedicants for outpatients include sedative-hypnotics, opioids, anticholinergics, antacids, gastrokinetics, H_2-receptor antagonists, and antiemetics. Most prospective studies have not found recovery to be prolonged after the use of appropriate doses of sedative premedication (e.g., midazolam 1 to 2 mg intravenous). Indeed, proper use of premedication may actually expedite the

discharge process as a result of its ability to reduce postoperative side effects. Clearly, however, lorazepam's very long duration of action makes it unsuitable for use in the ambulatory surgical patient.

Kain ZN, Sevarino F, Pincus S, et al. Attenuation of the preoperative stress response with midazolam: effects on postoperative outcomes. *Anesthesiology*. 2000;93:141.

Van Vlymen JM, SaRego MM, White PF. Benzodiazepine premedication: can it improve outcome in patients undergoing breast biopsy procedures? *Anesthesiology*. 1999;90:740.

B.11. Should every outpatient receive prophylaxis against acid aspiration pneumonitis?

Despite early studies demonstrating that a large percentage of outpatients are theoretically at risk for gastric aspiration, the actual incidence of pulmonary aspiration is very low (<1/35,000) in surgical patients with no specific risk factors. The possibility that outpatients have a greater potential for acid aspiration than inpatients had prompted several authors in the past to recommend that some form of aspiration prophylaxis be given to all patients scheduled for outpatient surgery. Unfortunately, this is costly and may result in undesired side effects. Although individual ambulatory surgery centers must determine their own policies, pharmacologic prevention of acid aspiration should not be routine, but rather reserved for outpatients with predisposing factors (e.g., pregnancy, symptomatic hiatal hernia, diabetes mellitus with autonomic neuropathy, morbid obesity). When antacids are used, they should be restricted to nonparticulate antacids.

Cohen NH. Aspiration: is there an optimal management strategy? In: Fleisher LA, ed. *Evidence-Based Practice of Anesthesiology*. 2nd ed. Philadelphia: Saunders Elsevier; 2009:327–332.

Lichtor JL. Ambulatory anesthesia. In: Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:833–846.

B.12. Is an overnight fast justified for all outpatients?

Several investigators have questioned the value of the traditional overnight fast for surgical outpatients, particularly pediatric outpatients. Prolonged fasting does not guarantee an empty stomach at the time of induction. It does, however, cause patient discomfort and may produce significant physiologic disturbances in infants and young children. Studies in children and in adults have shown no increase in volume or decrease in pH of gastric fluid when clear liquids were administered as late as 2 hours before induction of anesthesia. Therefore, arbitrary restrictions on the preoperative fast for surgical outpatients without risk factors for pulmonary aspiration, such as "NPO after midnight," appear to be unwarranted. Clear fluids in reasonable amounts (3 mL/kg) may be safely ingested until 2 hours before surgery. Although coffee is not transparent, it is devoid of particulate matter and is accepted as a clear liquid. There is some evidence that briefer periods of preoperative fasting (2 hours) are accompanied by less PONV, as well as a reduced incidence of dizziness, drowsiness, and thirst. Breast milk should be withheld for at least 4 hours in neonates and infants who are being breastfed. Intake of nonclear liquids, nonhuman milk, and solid food should be discontinued at least 6 hours before the induction of anesthesia.

Hall SC. The pediatric difficult airway: outpatient implications. In: Steele SM, Nielsen KC, Klein SM, eds. *Ambulatory Anesthesia & Perioperative Analgesia.* New York: McGraw-Hill; 2005:413–420.

Lichtor JL. Ambulatory anesthesia. In: Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia.* 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:833–846.

C. Intraoperative Management

C.1. What are the important considerations in choosing an anesthetic technique for outpatient surgery?

- Smooth and rapid onset of action
- Intraoperative amnesia and analgesia
- Hemodynamic stability
- Good operating conditions
- Rapid recovery period without side effects
- Cost-effectiveness

To date, no "ideal" anesthetic drug or technique has been identified for outpatients. No single agent or combination of agents, either inhaled or intravenous, has been clearly demonstrated to reduce recovery time and allow faster discharge of the ambulatory surgical patient. However, with its smooth induction profile and short elimination half-life, propofol may prove to be the induction, if not the maintenance, agent of choice for outpatient anesthesia. The newer halogenated ether compounds, sevoflurane and desflurane, have become increasingly popular in ambulatory anesthesia owing to their rapid onset and quick termination of clinical effects. Currently, desirable anesthetic conditions with an acceptable recovery profile may be produced by a large array of pharmacologically active drugs administered in conjunction with either general, regional, or local anesthesia techniques. It is essential, however, to combine these agents in a rational manner and carefully titrate them to optimal effect.

Gupta A, Fleisher LA. What outcomes are important in ambulatory anesthesia? In: Steele SM, Nielsen KC, Klein SM, eds. *Ambulatory Anesthesia & Perioperative Analgesia.* New York: McGraw-Hill; 2005:83–91.

Lichtor JL. Ambulatory anesthesia. In: Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia.* 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:833–846.

C.2. What are the anesthetic implications of recent retinal detachment surgery?

Patients who have had vitreoretinal surgery often have a gas bubble deliberately left within the eye to help tamponade and keep the retina attached as adhesions develop. Filtered room air, sulfur hexafluoride (SF_6), and perfluoropropane (C_3F_8) are the most commonly used gases. By varying the concentration, volume, and type of gas used, bubbles can be produced that will last up to 70 days before being completely absorbed. If nitrous oxide is administered during this time, the bubble will rapidly expand with the attendant risk of retinal and optic nerve ischemia secondary to central retinal artery occlusion. Primate models indicate that irreversible retinal damage occurs after 100 minutes of retinal artery obstruction, suggesting that perhaps some recovery might be expected after briefer anesthetics. However, a narrower window may exist in humans. Therefore, nitrous oxide should be avoided in any patient who

has undergone vitreoretinal surgery within the preceding 3 months, unless records are available to confirm that either intraocular gas was not used, or that it has subsequently been completely reabsorbed.

Hart RH, Vote BJ, Borthwick JH, et al. Loss of vision caused by expansion of intraocular perfluoropropane (C_3F_8) gas during nitrous oxide anesthesia. *Am J Ophthalmol*. 2002;134:761–763.

Hayreh SS, Kolder HE. Central retinal artery occlusion and retinal tolerance time. *Ophthalmology*. 1980;87:75–78.

Lee EJK. Use of nitrous oxide causing severe visual loss 37 days after retinal surgery. *Br J Anaesth*. 2004;93:464–466.

C.3. How would you monitor this patient?

The effects of anesthesia during ambulatory procedures should be monitored using the same standards applicable to inpatient procedures. Standard monitoring in this patient would include a blood pressure cuff, ECG, pulse oximeter, precordial or esophageal stethoscope, temperature probe, and measurement of inspired oxygen and end-tidal carbon dioxide. The potential for hypoxia and hypercarbia during laparoscopy requires careful monitoring of oxygen saturation and expired carbon dioxide tension. In addition, intra-abdominal pressure must be measured during gas insufflation into the peritoneal cavity. Although standard intraoperative monitoring is appropriate for most outpatients having laparoscopic surgery, ASA physical status III or IV patients may benefit from invasive hemodynamic monitoring to carefully and continuously determine the cardiovascular response to pneumoperitoneum and position changes.

Muir HA, Olufolabi AJ. Ambulatory anesthesia for laparoscopic surgery. In: Steele SM, Nielsen KC, Klein SM, eds. *Ambulatory Anesthesia & Perioperative Analgesia*. New York: McGraw-Hill; 2005:289–301.

C.4. What is the Bispectral Index (BIS) monitor and what information does it convey?

The BIS monitor is a noninvasive monitoring system that is derived from the electroencephalogram (EEG). Using bispectral analysis of the EEG waveform and other features within the EEG, the BIS monitor is used to detect changes in purported depth of anesthesia or hypnosis. A proprietary algorithm translates the complex data generated from the analysis of the EEG over a 30-second period into a single dimensionless number between 0 (i.e., no brain activity) and 100 (i.e., the patient is fully awake) that is displayed on the BIS monitor. The BIS is one of many brain function monitors that record or process brain electrical activity and convert these signals mathematically into a continuous measure, typically scaled from 0 to 100. It is important to appreciate that intraoperative awareness cannot be measured during the intraoperative phase of general anesthesia, because the recall component of awareness can only be determined postoperatively by obtaining information directly from the patient. Moreover, although clinically important, intraoperative awareness under general anesthesia is a rare occurrence, with a reported incidence of 0.1% to 0.2% in adults.

American Society of Anesthesiologists Task Force on Intraoperative Awareness. *Practice Advisory for Intraoperative Awareness and Brain Function Monitoring. A Report by the American Society of Anesthesiologists Task Force on Intraoperative Awareness*. Approved by the House of Delegates on October 25, 2005

Bergman IJ, Kluger MT, Short TG. Awareness during general anaesthesia: a review of 81 cases from the anaesthetic incident monitoring study. *Anaesthesia*. 2002;57:549–556.

Kent CD, Domino KB. Depth of anesthesia. *Curr Opin Anaesthesiol*. 2009;22:782–787.

Sebel PS, Bowdle TA, Ghoneim MM, et al. The incidence of awareness during anaesthesia: a multicenter United States study. *Anesth Analg*. 2004;99:833–839.

C.5. What benefits might be derived from using a BIS monitor?

Information about the patient's hypnotic state obtained from the BIS, in combination with other monitored parameters and clinical signs, may allow better balancing of hypnotic and analgesic administration. Titration of hypnotic agents based on individual requirements arguably is improved, potentially reducing the incidence of relative underdosing and overdosing. Furthermore, selection of anesthetic interventions (e.g., administration of hypnotics, analgesics, and vasoactive drugs) may be more rational. Reduced drug usage, earlier awakening, and faster recovery have all been associated with using the BIS monitor to help guide anesthesia maintenance. This translates into a higher potential for bypassing the stage 1 postanethesia care unit (PACU) and earlier discharge eligibility from the PACU. It is not known yet whether these benefits will ultimately reduce medical costs significantly. Indeed, a recent meta-analysis based on 1,380 subjects from 11 trials disclosed that BIS monitoring reduced anesthetic consumption by 19%, reduced the incidence of nausea/vomiting, and reduced time in the PACU by 4 minutes. However, these benefits did not lead to a significant reduction in time until patient discharge from the ambulatory surgery unit. Additionally, BIS monitoring actually increased the cost per patient by $5.55 owing to the cost of the BIS electrodes.

Recently, there has been considerable discussion about depth of anesthesia and 1-year mortality. The investigators in the B-Aware Trial reported their secondary analysis of long-term mortality and found that the absence of low BIS values (BIS <40 for >5 minutes) was associated with improved long-term survival and reduced morbidity (myocardial infarction, stroke). However, this putative association does not imply causation. Preoperative comorbidity is an important independent risk factor for postoperative mortality.

Johansen JW, Sebel PS. Development and clinical application of electroencephalographic bispectrum monitoring. *Anesthesiology*. 2000;93:1336–1344.

Leslie K, Myles PS, Forbes A, et al. The effect of bispectral index monitoring on long-term survival in the B-aware trial. *Anesth Analg*. 2010;110:816–822.

Liu S. Effects of bispectral index monitoring on ambulatory anesthesia: a meta-analysis of randomized controlled trials and a cost analysis. *Anesthesiology*. 2004;101:311–315.

O'Connor MF, Daves S, Tung A, et al. BIS monitoring to prevent awareness during general anesthesia. *Anesthesiology*. 2001;94:520–522.

Pavlin JD, Souter KJ, Hong JY. Effects of bispectral index monitoring on recovery from surgical anesthesia in 1,580 inpatients from an academic medical center. *Anesthesiology*. 2005;102:566–573.

C.6. Is BIS monitoring applicable to children?

The BIS was developed and tested on adults. Because the EEG in infants and young children is different from that of an adult and changes as the brain matures, the BIS value may not necessarily apply to the pediatric patient population. Validating the BIS monitor in infants and young children poses significant problems. End points used to confirm BIS in adults, such as assessment of sedation, sleep, or purposeful movement

in response to voice commands, cannot be reliably obtained in young children. Furthermore, there are serious ethical problems in recruiting healthy children as volunteers in studies of general anesthesia. Nevertheless, recent data from numerous authors comparing BIS values between adults and children at various clinical end points during general anesthesia, such as before anesthesia, during maintenance, at emergence, and with increasing concentrations of volatile anesthetic, suggest that BIS generally performs similarly in adults and children with respect to dose response to anesthetic agents. However, a recent study disclosed that in children aged 6 months to 12 years, the BIS increased paradoxically as end-tidal sevoflurane concentration increased from 3% to 4%. BIS values showed a wide variation at the same end-tidal sevoflurane concentration, and the age of the patient was considered to be a factor affecting the BIS values. A consensus seems to be forming that BIS monitoring should be used with caution in infants less than 1 year of age. Clearly, further work in this area is needed. Definitive studies correlating level of sedation, awareness, and anesthetic outcome with BIS in children have not yet been published. Nonetheless, consensus is emerging that the incidence of intraoperative awareness is greater in children than in adults. Children, however, seem to be less disturbed by the experience than adults who appear to be more vulnerable to the development of posttraumatic stress.

Bannister CF, Brosius KF, Sigl JC, et al. The effect of bispectral index monitoring on anesthetic use and recovery in children anesthetized with sevoflurane in nitrous oxide. *Anesth Analg*. 2001;92:877–881.

Blussé van Oud-Alblas HJ, Van Dijk M, Liu C, et al. Intraoperative awareness during paediatric anaesthesia. *Br J Anaesth*. 2009;102:104–110.

Davidson AJ, Huang GH, Czarnecki C, et al. Awareness during anesthesia in children: a prospective cohort study. *Anesth Analg*. 2005;100:653–661.

Davidson AJ, Huang GH, Rebmann CS, et al. Performance of entropy and bispectral index as measures of anaesthesia effect in children of different ages. *Br J Anaesth*. 2005;95:674–679.

Kim HS, Oh AY, Kim CS, et al. Correlation of bispectral index with end-tidal sevoflurane concentration and age in infants and children. *Br J Anaesth*. 2005;95:363–366.

C.7. What are the major limitations of BIS monitoring?

The BIS monitor is not a measure of global anesthetic depth. It is only a measure of the patient's level of sedation and hypnotic state. As such, it helps the anesthesiologist assess the potential for patient awareness, but it cannot prevent it. In fact, use of the BIS has not been proved to reduce or eliminate the risk of intraoperative awareness. The BIS will not predict patient movement or hemodynamic response to noxious stimulation, nor will it predict the exact moment when consciousness will return. Sedation produced by both ketamine and nitrous oxide does not produce the expected decrease in BIS. The utility of BIS in patients with neurologic disease has not been adequately studied to validate its use in these patients. Finally, more work is necessary to establish whether BIS is an accurate measure of hypnosis in pediatric patients.

It is important to appreciate that a specific numerical value may not correlate with a specific depth of anesthesia. Moreover, the measured values do not have uniform sensitivity across different anesthetic drugs or types of patients. Artifacts may be introduced by electrocautery, lasers, warming devices, and other devices and circumstances. The BIS cannot be relied upon in all situations, including hypothermia, circulatory arrest, and brain death. Moreover, one small study recently reported that patient position may affect BIS readings, with the head-down position producing an increase in BIS value, and the head-up position being associated with a reduction in BIS value. Clearly, intraoperative monitoring of depth of anesthesia to minimize the

risk of awareness should rely on multiple modalities, including clinical observations of purposeful or reflex movement, ECG tracing, blood pressure, heart rate, end-tidal anesthetic analyzer, and capnography.

The consensus of the ASA Task Force on Intraoperative Awareness is that brain function monitoring is not routinely indicated for patients undergoing general anesthesia, and that the decision to use a brain function monitor should be made on a case-by-case basis by the individual practitioner for selected patients at increased risk.

American Society of Anesthesiologists Task Force on Intraoperative Awareness. *Practice Advisory for Intraoperative Awareness and Brain Function Monitoring. A Report by the American Society of Anesthesiologists Task Force on Intraoperative Awareness.* Approved by the House of Delegates on October 25, 2005.

Avidan MS, Zhang L, Burnside BA, et al. Anesthesia awareness and the bispectral index. *N Engl J Med.* 2008;358:1097–1108.

Barr G, Jakobsson JG, Öwall A, et al. Nitrous oxide does not alter bispectral index: study with nitrous oxide as sole agent and as adjunct to i.v. anaesthesia. *Br J Anaesth.* 1999;82:827–830.

Chan MTV, Gin T. What does the bispectral EEG index monitor? *Eur J Anaesthesiol.* 2000;17:146–148.

Kaki AM, Almarakbi WA. Does patient position influence the reading of the bispectral index monitor? *Anesth Analg.* 2009;109:1843–1846.

Wennervirta J, Salmi T, Hynynen M, et al. Entropy is more resistant to artifacts than bispectral index in brain-dead organ donors. *Intensive Care Med.* 2007;33:133–136.

C.8. What does a BIS reading of 56 mean?

The BIS scale is a dimensionless scale from 0 to 100. Typically, BIS values between 40 and 60 correspond with a moderate hypnotic state of general anesthesia, and are associated with a low probability of patient consciousness. Deep sedation with a low probability of explicit recall occurs in the 60 to 70 BIS range, with higher values up to 85 associated with light to moderate sedation. A BIS number below 40 indicates a deep hypnotic state, with brain isoelectricity increasing as BIS approaches 0. As mentioned previously, however, there are multiple exceptions to these generalities, and the BIS is perhaps best thought of as a trend monitor rather than an "absolute" monitor of hypnotic depth.

Hemmerling TM, Migneault B. Falsely increased bispectral index during endoscopic shoulder surgery attributed to interferences with the endoscopic shaver device. *Anesth Analg.* 2002;95:1678–1679.

Johansen JW, Sebel PS. Development and clinical application of electroencephalographic bispectrum monitoring. *Anesthesiology.* 2000;93:1337.

C.9. What are the anesthetic options for laparoscopy?

In recent years, anesthesiologists have successfully employed local, regional, and general anesthesia for laparoscopy. Local and regional anesthesia offer the potential advantages of faster postoperative recovery and reduced postoperative complications. These techniques also avoid the postoperative discomforts of general anesthesia, such as sore throat, muscle pains, and airway trauma. However, steep Trendelenburg position, pneumoperitoneum, and surgical manipulation often make spontaneous ventilation difficult during local or regional anesthesia. In addition, the potential for postspinal headache and urinary retention may detract from the use of regional

anesthesia in the outpatient. The vast majority of laparoscopic procedures continue to be performed under general endotracheal anesthesia. General anesthesia offers the advantages of elimination of patient anxiety, complete amnesia and analgesia, the ability to control ventilation, muscle relaxation, and a motionless operative field.

Muir HA, Olufolabi AJ. Ambulatory anesthesia for laparoscopic surgery. In: Steele SM, Nielsen KC, Klein SM, eds. *Ambulatory Anesthesia & Perioperative Analgesia.* New York: McGraw-Hill; 2005:289–301.

C.10. Under what circumstances might spinal anesthesia be appropriate for outpatient laparoscopy?

The use of regional anesthesia for laparoscopic surgery is not widely practiced in the United States. However, selective spinal anesthesia has been described in several publications. This method is defined as the practice of using minimal doses of dilute intrathecal agents in order to anesthetize only the nerve roots supplying a specific area and to affect only the modalities that need to be affected. Many of these publications have involved the use of hypobaric solutions of 10 mg lidocaine with the addition of 10 μg fentanyl for gynecologic laparoscopy. This solution purportedly gives good to excellent operating conditions with minimal motor block and a brief recovery period. Typically, dorsal column function, proprioception, and touch remain intact perioperatively. Transient neurologic symptoms have not been reported with the use of 10 mg hypobaric lidocaine with fentanyl, but transient neurologic symptoms have been reported in conjunction with 20 mg intrathecal lidocaine. Recently, low-dose 3 mg levobupivacaine plus 10 μg fentanyl has been used successfully for selective spinal anesthesia in gynecologic outpatient laparoscopy. Clearly, this approach is best used for brief procedures where the surgeon does not require steep Trendelenburg positioning.

Ben-David B, Maryanovsky M, Gurevitch A, et al. A comparison of minidose lidocaine-fentanyl and conventional-dose lidocaine spinal anesthesia. *Anesth Analg*. 2000; 91:865–870.

De Santiago J, Santos-Yglesias J, Giron J, et al. Low-dose 3 mg levobupivacaine plus 10 μg fentanyl selective spinal anesthesia for gynecological outpatient laparoscopy. *Anesth Analg*. 2009;109:1456–1461.

Vaghadia H, Viskari D, Mitchell GWE, et al. Selective spinal anesthesia for outpatient laparoscopy. I: characteristics of three hypobaric solutions. *Can J Anaesth*. 2001;48:256–260.

C.11 What anesthetic agents would you use to induce and maintain general anesthesia in this patient?

A number of anesthetic agents in a variety of combinations can be used successfully to provide general anesthesia in this patient. A reasonable approach would be to induce anesthesia with propofol or a short-acting barbiturate, such as sodium thiopental, after a preinduction dose of a short-acting benzodiazepine. After intubation, anesthesia is maintained with a volatile anesthetic, such as sevoflurane or desflurane, and an air–oxygen mixture, supplemented with a short-acting narcotic as needed and a muscle relaxant. Alternatively, a total intravenous technique with propofol as the primary agent could be administered.

Muir HA, Olufolabi AJ. Ambulatory anesthesia for laparoscopic surgery. In: Steele SM, Nielsen KC, Klein SM, eds. *Ambulatory Anesthesia & Perioperative Analgesia.* New York: McGraw-Hill; 2005:289–301.

C.12. Would you avoid the use of nitrous oxide in this ambulatory patient?

As mentioned in the preceding text, if the patient has an intraocular gas bubble that is not completely resorbed, nitrous oxide is contraindicated for fear of causing devastating visual damage. In the absence of this contraindication, the use of nitrous oxide, albeit somewhat controversial, could be considered. Traditionally, there had been concerns about its ability to diffuse into bowel lumen causing distension and to increase postoperative nausea/vomiting. It has been shown that surgical conditions during laparoscopic procedures lasting 70 to 80 minutes were identical (bowel distension did not increase over time) regardless of whether nitrous oxide was used. In a laboratory study involving porcine subjects, nitrous oxide was shown to diffuse into a carbon dioxide peritoneum and the nitrous oxide fraction exceeded 29%, a level that can support combustion, within 2 hours. Therefore, the clinical risk associated with prolonged laparoscopy remains unclear. Although it had historically been held that nitrous oxide can contribute to PONV, conclusive evidence is lacking to demonstrate an important effect of nitrous oxide on the incidence of postoperative emesis after laparoscopic cholecystectomy or pelvic laparoscopy. Therefore, any potential benefit from its elimination must be balanced against the potential increased risk of intraoperative awareness.

Cunningham AJ, Nolan C. Anesthesia for minimally invasive procedures. In: Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2006:1065–1066.

Diemunsch PA, Torp KD, Van Dorsselaer T, et al. Nitrous oxide fraction in the carbon dioxide pneumoperitoneum during laparoscopy under general inhaled anesthesia in pigs. *Anesth Analg*. 2000;90:951.

Taylor E, Feinstein R, White PF. Anesthesia for laparoscopic cholecystectomy: is nitrous oxide contraindicated? *Anesthesiology*. 1992;76:561.

C.13. Discuss the physiologic changes induced by laparoscopy.

Physiologic changes occur as a result of the pneumoperitoneum and the Trendelenburg position that are required during laparoscopy. Carbon dioxide or nitrous oxide can be used to produce the pneumoperitoneum. Insufflation of gas into the peritoneal cavity elevates intra-abdominal pressure and impairs venous return. As intra-abdominal pressure increases above 20 mm Hg, central venous pressure, arterial pressure, pulse pressure, and cardiac output all decrease. Although rare, severe hypotension and cardiac arrest have been reported. The pneumoperitoneum also sequesters blood in the legs, thereby decreasing the circulating blood volume. Vital capacity is significantly reduced as the diaphragm is displaced cephalad by the Trendelenburg position and pneumoperitoneum. Pulmonary compliance is decreased, functional residual capacity is diminished, and aeration of the lower lobes is compromised, predisposing the patient to the development of hypoxia and atelectasis. As the intraperitoneal gas is released and intra-abdominal pressure decreases, all cardiovascular and respiratory parameters should return to normal.

Cunningham AJ, Nolan C. Anesthesia for minimally invasive procedures. In: Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2006:1062–1065.

Muir HA, Olufolabi AJ. Ambulatory anesthesia for laparoscopic surgery. In: Steele SM, Nielsen KC, Klein SM, eds. *Ambulatory Anesthesia & Perioperative Analgesia*. New York: McGraw-Hill; 2005:289–301.

C.14. In addition to the physiologic changes described in the preceding text, what other intraoperative complications are associated with laparoscopy?

Absorption of carbon dioxide used for peritoneal insufflation may produce hypercarbia, resulting in hypertension, hypotension, catecholamine stimulation, cardiac arrhythmias, and acidosis. Arrhythmias may also be produced by vasovagal reflexes. Hemorrhage accounts for nearly half of the complications from laparoscopy. Bowel injury and ischemia can occur. A cephalad shift of the mediastinum may cause the endotracheal tube to pass into a bronchus after the Trendelenburg position is assumed. Other complications include gas embolization, tension pneumothorax, pneumomediastinum, perforation and electrical injury of organs, and passive regurgitation and aspiration.

Cunningham AJ, Nolan C. Anesthesia for minimally invasive procedures. In: Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2006:1062–1067.

Kim CS, Kim JY, Kwon J-Y, et al. Venous air embolism during total laparoscopic hysterectomy: comparison to total abdominal hysterectomy. *Anesthesiology*. 2009;111:50–54.

Muir HA, Olufolabi AJ. Ambulatory anesthesia for laparoscopic surgery. In: Steele SM, Nielsen KC, Klein SM, eds. *Ambulatory Anesthesia & Perioperative Analgesia*. New York: McGraw-Hill; 2005:289–301.

C.15. Why is carbon dioxide the insufflation agent of choice for laparoscopy?

Carbon dioxide is the most commonly used agent for laparoscopy because it is more soluble in blood than air, oxygen, or nitrous oxide. The carbon dioxide–carrying capacity of the blood is high, owing to bicarbonate buffering and combination with hemoglobin and plasma proteins. Rapid elimination also increases the margin of safety in the event of intravenous injection of carbon dioxide. All of these properties contribute to the rapid reversal of the clinical signs of carbon dioxide embolism when treated properly. Therefore, the lethal dose of carbon dioxide is approximately five times greater than that of air.

Muir HA, Olufolabi AJ. Ambulatory anesthesia for laparoscopic surgery. In: Steele SM, Nielsen KC, Klein SM, eds. *Ambulatory Anesthesia & Perioperative Analgesia*. New York: McGraw-Hill; 2005:289–301.

Wolf JS Jr, Carrier S, Stoller ML. Gas embolism: helium is more lethal than carbon dioxide. *J Laparoendosc Surg*. 1994;4:173.

C.16. What are some alternatives to carbon dioxide for laparoscopy?

Insufflation of inert gases, such as helium or argon, instead of carbon dioxide avoids the increase in $Paco_2$ from absorption, thereby avoiding the need for hyperventilation. The ventilatory consequences of the increased intra-abdominal pressure persist, however. Although the hemodynamic consequences of pneumoperitoneum from inert gases are similar to those seen with carbon dioxide, the inert gases blunt the increase in arterial pressure but exacerbate the decrease in cardiac output. Unfortunately, the low blood solubility of the inert gases is concerning in the event of gas embolism.

Gasless laparoscopy, using abdominal wall lift from a fan retractor, is another alternative to carbon dioxide. This technique may be attractive for patients with severe cardiac or pulmonary disease because it avoids the respiratory and hemodynamic consequences

of increased intra-abdominal pressure secondary to insufflation. However, gasless laparoscopy compromises surgical exposure and exacerbates technical difficulty.

Goldberg JM, Maurer WG. A randomized comparison of gasless laparoscopy and CO_2 pneumoperitoneum. *Obstet Gynecol*. 1997;90:416.

Wolf JS Jr, Carrier S, Stoller ML. Gas embolism: helium is more lethal than carbon dioxide. *J Laparoendosc Surg*. 1994;4:173.

D. Postoperative Management

D.1. What are the common causes of nausea and vomiting in outpatients?

Nausea and vomiting are significant problems after ambulatory surgery, causing patient discomfort and delayed recovery and discharge from the ambulatory center. Prolonged vomiting is one of the most frequent causes of unexpected hospital admission from the ambulatory surgical facility and is a major cause of patients' dissatisfaction with their anesthesia care. Patients who have a history of motion sickness and a previous experience of PONV are more likely to develop postoperative emetic symptoms, as are patients who are obese or pregnant or have diabetes mellitus. PONV are common in children; the incidence decreases with age. Men and women are equally affected until puberty, when the incidence becomes considerably higher in women. Excessive anxiety and noncompliance with fasting can increase gastric volume and predispose patients to PONV. Interestingly, smoking has been shown to decrease the incidence of PONV.

The use of narcotic analgesics, particularly morphine and meperidine, as premedication, as part of the anesthetic technique, or postoperatively to control pain, increases the incidence of PONV after outpatient anesthesia. Methohexital is less likely than either thiopental or etomidate to cause postoperative nausea. Consistently, propofol was shown to have a low incidence of emetic symptoms postoperatively.

Although Apfel's scoring system to predict the likelihood of PONV emphasizes female gender, nonsmoking status, history of PONV or motion sickness, and narcotic administration as the major risk factors, Sinclair also identifies surgical issues. Surgical procedures such as breast augmentation, varicose vein stripping, laparoscopy, dilatation and curettage, strabismus correction, myringotomy and tympanostomy tube placement, and orchiopexy are associated with more PONV, with the incidence escalating with increasing surgical and anesthesia time. A recent study by Ruiz et al. found that the type of surgery, when categorized anatomically, was related to the incidence of PONV, with patients having neurologic, head or neck, and abdominal surgery having the greatest likelihood of experiencing emesis in the postanesthesia care unit. In addition, pain, hypotension, and early ambulation are postoperative factors demonstrated to increase nausea and vomiting. Relief of pain often, but not always, relieves concomitant nausea.

Apfel C, Kranke P, Eberhart LHJ, et al. Comparison of predictive models for postoperative nausea and vomiting. *Br J Anaesth*. 2002;88:234–240.

Apfel CC, Laara E, Koivuranta M, et al. A simplified risk score for predicting postoperative nausea and vomiting: conclusions from cross validation between two centers. *Anesthesiology*. 1999;91:693.

Ruiz JR, Kee SS, Frenzel JC, et al. The effect of an anatomically classified procedure on antiemetic administration in the postanesthesia care unit. *Anesth Analg*. 2010;110:403–409.

Sinclair DR, Chung F, Mezei G. Can postoperative nausea and vomiting be predicted? *Anesthesiology*. 1999;91:109–118.

D.2. How would you pharmacologically prevent PONV in the susceptible ambulatory patient?

Because of concerns about medication cost and potential side effects, routine prophylactic administration of an antiemetic is not considered appropriate for all ambulatory surgical patients. Instead, antiemetic prophylaxis should be reserved for patients who are considered to be susceptible to developing PONV (see preceding text). A large number of medications have been used to prevent postanesthetic nausea and vomiting in the outpatient, some with only limited success. Unfortunately, the ideal medication for each patient is not known. Serotonin antagonists, such as ondansetron 4 to 8 mg intravenous in adults and 0.1 mg per kg intravenous in children, are highly effective, but their use as single agents in high-risk patients may not suffice. Droperidol has been shown to be effective, inexpensive, and without an increase in postoperative sedation when used in low doses, such as 0.625 to 1.25 mg in adults (or as low as 10 to 20 μg per kg). However, the U.S. Food and Drug Administration issued a so-called black box warning on the use of droperidol for antiemetic prophylaxis owing to purported fears about prolongation of the QTc interval and subsequent potentially dangerous ventricular arrhythmias. Nonetheless, Charbit et al. documented that droperidol and ondansetron induce similar clinically relevant QTc prolongation, and concluded that the safety of 5-hydroxytryptamine type 3 (5-HT_3) antagonists may not be superior to that of low-dose droperidol. Although the serotonin antagonists are classically believed to lack efficacy with regard to preventing or treating nausea, the newest 5-HT_3 blocker, palonosetron, appears to reduce its severity, and the extended benefits of palonosetron may last up to 3 days, given its long half-life. In addition, palonosetron purportedly has no QT interval issues.

Prophylactic administration of dexamethasone, 5 to 10 mg intravenous in adults and 0.5 to 1 mg per kg intravenous in children, is effective in the prevention of PONV and appears to offer no evidence of any clinically relevant toxicity. Combining dexamethasone with a serotonin antagonist further decreases the incidence of nausea and vomiting and may prove to be the best prophylactic regimen, although optimal doses of this combination are not currently known. Transdermal scopolamine effectively reduces PONV if given as a premedicant well in advance of the surgery, but the high incidence of anticholinergic side effects and prolonged residual effects on cognitive performance, especially in the elderly, detract from its usefulness in the ambulatory patient.

Aprepitant is a highly selective, brain-penetrating neurokinin_1 receptor antagonist that is effective against centrally induced emesis. A recent study showed that aprepitant was superior to ondansetron for prevention of vomiting in the first 24 to 48 hours, but no notable differences were detected between aprepitant and ondansetron for nausea control, use of rescue drugs, or complete response.

Because the etiology of PONV is multifactorial, there is increasing evidence that a multimodal approach may lead to improved outcomes. Double and triple antiemetic combinations, using drugs with different mechanisms of action, are recommended for patients at high risk of PONV. Moreover, liberal hydration and effective analgesia play an important role in reducing the incidence of PONV. General anesthesia with volatile agents should be avoided, if possible, in high-risk patients. If general anesthesia is necessary, a total intravenous approach with propofol may be advantageous. Moreover, if rescue therapy for PONV is needed within 6 hours of surgery, patients should not receive a repeat dose of the drug that was administered prophylactically. Rather, a rescue drug with a different mechanism of action should be selected.

Apfel CC, Katz MH, Kranke P, et al. Volatile anesthetics may be the main cause of early but not delayed postoperative vomiting: a randomized controlled trial of factorial design. *Br J Anaesth*. 2002;88:659–668.

Charbit B, Albaladejo P, Funck-Brentano C, et al. Prolongation of QTc interval after postoperative nausea and vomiting treatment by droperidol or ondansetron. *Anesthesiology*. 2005;102:1094–1100.

Gan TJ, Apfel CC, Kovac AL, et al. A randomized, double-blind comparison of the NK_1 receptor antagonist, aprepitant, versus ondansetron for the prevention of postoperative nausea and vomiting. *Anesth Analg*. 2007;104:1082–1089.

Gan TJ, Meyer T, Apfel CC, et al. Society for Ambulatory Anesthesia guidelines for the management of postoperative nausea and vomiting. *Anesth Analg*. 2007;105:1615–1628.

Kovac AL, Eberhart L, Kotarski J, et al. A randomized, double-blind study to evaluate the efficacy and safety of three different doses of palonosetron versus placebo in preventing postoperative nausea and vomiting over a 72-hour period. *Anesth Analg*. 2008;107:353–355.

Scuderi PE, James RL, Harris L, et al. Multimodal antiemetic management prevents early postoperative vomiting after outpatient laparoscopy. *Anesth Analg*. 2000;91:1408–1414.

D.3. How is postoperative pain treated?

Pain control is one of the most important factors in determining when a surgical outpatient can be discharged. Pain should be treated rapidly and effectively to minimize postoperative symptoms so that ambulation and discharge are not delayed. The optimal strategy is to use a preemptive, multimodal approach. Begin controlling postoperative pain intraoperatively by supplementing the anesthetic technique with a short-acting narcotic analgesic or a regional block. Intravenous fentanyl is usually the drug of choice for postoperative pain relief. It may be given in small doses of 12.5 μg at 5-minute intervals and titrated to relief of pain. Ketorolac, a nonsteroidal anti-inflammatory drug, has become increasingly popular in the management of postoperative pain in the ambulatory patient because of its lack of opioid-related side effects (e.g., sedation, nausea, vomiting, respiratory depression). It is available for oral and parental administration, and its use may decrease a patient's requirement for opioid analgesics. Controversy still surrounds the perioperative use of ketorolac because of the potential for bleeding complications and renal dysfunction. Local and regional anesthetic techniques can be used to provide effective postoperative analgesia, and when used to supplement general anesthesia, facilitate a pleasant emergence and minimize the need for opioids. Commonly used techniques include local infiltration of the incision site, intra-articular injection, nerve blockade (e.g., dorsal nerve penile block for circumcision, or ilioinguinal and iliohypogastric nerve blocks for inguinal hernia repair), and caudal blocks. When the patient has resumed intake of oral fluids, oral analgesics (e.g., acetaminophen, nonsteroidal anti-inflammatory drugs, as well as codeine and other opioid analgesics) may be administered for control of pain after discharge.

Lichtor JL. Ambulatory anesthesia. In: Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009: 833–846.

D.4. If the patient complained of eye pain postoperatively, how would you manage the situation?

Pain due to corneal abrasion is the most common ocular complication of general anesthesia. Patients with a corneal abrasion usually complain of a foreign body sensation, pain, tearing, and photophobia. The pain is typically exacerbated by blinking and ocular movement. It is wise to have an ophthalmologic consultation immediately. Treatment typically consists of the prophylactic application of antibiotic ointment and patching the injured eye shut. Although permanent sequelae are possible, healing usually occurs within 24 hours.

If the patient complains of intense pain, he or she should be scrupulously observed for signs of red eye, corneal edema, and a fixed mid-dilated pupil, as well as complaints of blurred vision. These are characteristic signs of acute angle-closure glaucoma (ACG), a serious emergency. Ophthalmologic consultation should be secured immediately to acutely decrease intraocular pressure (IOP) with systemic and topical therapy. Topical pilocarpine 2% is administered to cause miosis and pull the iris taut and away from the trabecular meshwork. A topical β-blocker also should be considered. If a prompt reduction in IOP does not ensue, systemic therapy with an agent such as mannitol should be considered, but its potentially adverse hemodynamic effects should be weighed in a patient with cardiovascular disease. If medical therapy is effective in reducing IOP to a safe level and the angle opens, an iridotomy/iridectomy can be performed immediately, or it can be delayed until the corneal edema resolves and the iris becomes less hyperemic. Failure to act effectively and expeditiously in cases of ACG could result in blindness. The excruciating periorbital pain typically described in these patients is an important aid in differential diagnosis.

Patients with open-angle glaucoma can also experience an acute glaucoma attack after surgery, but the IOP tends to be lower than that seen with ACG. The eye characteristically appears pale, dry, and firm, and the patient generally complains of a dull, periorbital headache. Treatment includes topical miotics and 5 to 7 mg per kg of acetazolamide intravenously. If the patient does not respond to medical therapy, laser trabeculoplasty may be necessary. Should laser treatment be ineffective, conventional filtration surgery, placement of a Molteno valve, or a coablative procedure may be indicated.

McGoldrick KE, Gayer SI. Anesthesia for ophthalmologic surgery. In: Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:1321–1345.

McGoldrick KE, Kosarussavadi B. Increased intraocular pressure. In: Atlee JL, ed. *Complications in Anesthesia*. Philadelphia: WB Saunders; 1999:765–768.

D.5. What criteria would you use to establish that a patient can be safely discharged after ambulatory surgery?

For patients to be discharged from an ambulatory facility, they must satisfy specific criteria that are usually summarized on simplified checklists. Although each ambulatory surgical facility must determine its own set of criteria, generally accepted guidelines for safe discharge home after ambulatory surgery include the following:

- Stable vital signs
- No evidence of respiratory depression
- Oriented to person, place, and time
- Able to walk unassisted
- Able to dress unassisted
- Minimal nausea or vomiting
- No active bleeding or oozing
- Pain controllable with oral analgesics
- Responsible adult to escort patient home, and to remain with the patient overnight
- Discharge by both the person who administered anesthesia and the person who performed surgery, or their designees. Written instructions for the postoperative period at home must be supplied to the patient before discharge, as well as a phone number to call in the case of emergency

The requirement for patients to drink and void before discharge is no longer considered mandatory, except in the case of certain patients who had central neuraxial blockade (see subsequent text).

Lichtor JL. Ambulatory anesthesia. In: Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:833–846.

Marshall SI, Chung F. Discharge criteria and complications after ambulatory surgery. *Anesth Analg*. 1999;88:514.

D.6. How would you decide when to discharge a patient after regional anesthesia?

Patients recovering from regional anesthesia must satisfy the discharge criteria listed in the preceding text. In addition, if spinal or epidural anesthesia has been used for outpatients, it is important to ensure recovery from the sympathetic and the motor blocks. Hypotension and syncope on standing may be signs that the sympathetic nervous system is still blocked. An indication that the motor block is no longer functioning is the ability to move the legs and feet freely. A simple test is to have the patient run each heel up and down the opposite leg from the big toe to the knee. A patient's ability to walk to the bathroom and void are excellent recovery tests after epidural or spinal anesthesia, because these abilities reflect recovery of both the motor and the sympathetic functions.

Recently, Mulroy et al. have suggested that delaying discharge for voiding after spinal or epidural anesthesia with *short-acting local anesthetics* is unnecessary in *low-risk* patients (e.g., age younger 70 years; no hernia, rectal, or urologic surgery; no history of voiding problems). Nonetheless, appropriate measures must be in place for bladder catheterization if the inability to void persists after discharge home. The use of ultrasonographic monitoring of bladder volume before discharge may reduce the incidence of urinary retention after the patient returns home.

Darrah DM, Griebling TL, Silverstein JH. Postoperative urinary retention. *Anesthesiol Clin*. 2009;27(3):465–484.

Marshall SI, Chung F. Discharge criteria and complications after ambulatory surgery. *Anesth Analg*. 1999;88:511–512.

Mulroy MF, Salinas FV, Larkin KL. Ambulatory surgery patients may be discharged before voiding after short-acting spinal and epidural anesthesia. *Anesthesiology*. 2002;97:315.

Pavlin JD, Pavlin EG, Gunn HC, et al. Voiding in patients managed with or without ultrasound monitoring of bladder volume after outpatient surgery. *Anesth Analg*. 1999;89:90–97.

D.7. What instructions should be given to an ambulatory surgical patient upon discharge?

Patients should be discharged to the care of a responsible adult. Additionally, they should be instructed that after surgery, they should not ingest an alcoholic beverage or depressant medication unknown to their surgeon or anesthesiologist, drive a car, or operate complex machinery for at least 24 hours. In addition, the discharge instructions should provide a list of problems that require immediate notification of the surgeon (e.g., bleeding that does not stop, inability to void, and persistent PONV.

Lichtor JL. Ambulatory anesthesia. In: Barash PG, Cullen BF, Stoelting RK, et al., eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:833–846.

Marshall SI, Chung F. Discharge criteria and complications after ambulatory surgery. *Anesth Analg*. 1999;88:514.

CHAPTER 61

Magnetic Resonance Imaging

JUNG HEE HAN

A 2-YEAR-OLD BOY weighing 15 kg is scheduled for a preoperative magnetic resonance imaging (MRI) of his brain for ongoing seizures with possible craniotomy with intraoperative MRI the following week. The technician reports that an attempt to obtain a scan last week was unsuccessful because of patient movement despite adequate sedation by the pediatrician. The child's past medical history is remarkable for partial tonic-clonic seizures since age 1. The child was born full term with no complications at birth and is otherwise healthy. Medications include carbamazepine and valproic acid, both of which were taken the night prior. NPO (nothing orally) status has been maintained for at least 6 hours.

A. Medical Disease and Differential Diagnosis

1. What is magnetic resonance imaging (MRI) and how does it work?
2. What are some advantages of MRI?
3. What are some disadvantages associated with MRI? What are some safety concerns?
4. What are the contraindications to MRI?
5. What are the biologic effects of clinical MRI?
6. What are the anesthetic considerations for this procedure?
7. What is intraoperative MRI?

B. Preoperative Evaluation and Preparation

1. What type of patients may require sedation or general anesthesia for a magnetic resonance examination?
2. What preoperative laboratory testing would you require for this patient?
3. How would you premedicate this patient?

C. Intraoperative Management

1. What are some of the anesthetic options for this patient?
2. How is an MRI conducted?
3. How would you monitor this patient?
4. What special considerations apply to the monitoring equipment used during MRI?
5. How would you induce and maintain general anesthesia in this patient?
6. How would you maintain the airway during the scan?
7. What is the laryngeal mask airway (LMA)?
8. What are the advantages of the LMA compared with the face mask?
9. What are the advantages of the LMA compared with the endotracheal tube (ETT)?
10. What complications are associated with the use of the LMA?
11. What are contraindications to the use of the LMA?
12. What are indications for the use of the LMA?
13. What size LMA is appropriate for this child, and how much air would routinely be required to properly inflate the cuff?
14. How is the LMA prepared?
15. How is the LMA inserted?
16. What additional maneuvers may be attempted if difficulty is encountered when inserting the LMA?
17. Examination of the patient before the table is fed into the MRI scanner reveals wheezing. What most likely is happening, and what do you do?
18. Discuss how the LMA can be used as a conduit for tracheal intubation.
19. Discuss the uses of the LMA in the patient with a difficult airway.

D. Postoperative Management

1. When is the LMA removed?
2. How will you have the patient recover from anesthesia?

A. Medical Disease and Differential Diagnosis

A.1. What is magnetic resonance imaging (MRI), and how does it work?

MRI is a noninvasive diagnostic technique that uses magnetic properties of atomic nuclei to produce high-resolution, multiplanar cross-sectional images of the body. Atoms having an odd number of protons and/or neutrons in their nuclei have an associated electrical charge, and the net rotation of protons or neutrons produces a local magnetic field similar to the electromagnetic field produced by the flow of electrons in a wire loop. Normally, the magnetic fields surrounding these nuclei are randomly oriented. When placed in the powerful static magnetic field of the MRI scanner, the nuclei align themselves longitudinally so they lie parallel or antiparallel to the magnetic field.

Within the MRI, a specific RF pulse of energy (a second magnetic field) is directed toward the patient at right angles to the static magnetic field, thereby displacing the orientation of the aligned nuclei from the longitudinal magnetic field. As the RF pulse is removed, the nuclei return to their original magnetic alignment positions. This is termed *relaxation*. The energy released from the tissue as the nuclei relax is termed an RF signal. It can be detected by the receiver coil of the scanner and used to produce the magnetic resonance image. There are two ways to measure relaxation

time. T1 relaxation represents the time to revert to the resting magnetic state and T2 relaxation represents the time to revert to the resting axial spin. The time it takes for relaxation to occur varies for specific body tissues, especially water and fat. This allows for differentiation of body structures, as well as between normal and pathologic tissue. Different atoms respond to different radiofrequencies, with the response being proportional to the strength of the static magnetic field. Hydrogen is present in high concentrations in biologic tissues and is the atom most often used for imaging. Resolution of the image requires a strong magnetic field. The magnetic field strength used to quantify the scanners is in tesla units. One tesla is equivalent to 10,000 gauss. Most MRI scanners used now have a magnetic field of 0.5 to 3.0 T (the magnetic field of the earth is 5×10^{-5} T). Some research scanners are 8.0 T. Weaker field scanners have the advantage of being an open construction whereas the stronger ones generate better image quality. The magnetic field of an MRI takes several days to establish. Therefore, it is constantly applied even in the absence of a patient, and it is deactivated only in an emergency.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:868.

Menon DK, Peden CJ, Hall AS. Magnetic resonance for the anaesthetist. Part I. Physical principles, applications, safety aspects. *Anaesthesia*. 1992;47:241–242.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier, Churchill Livingstone; 2010:2466–2467.

Patteson SK, Chesney JT. Anesthetic management for magnetic resonance imaging: problems and solutions. *Anesth Analg*. 1992;74:121–122.

A.2. What are some advantages of MRI?

The advantages of MRI include the lack of ionizing radiation, the capability of using noniodinated intravenous contrast agent, and the production of multiplanar images. MRI also provides excellent resolution of normal tissues (e.g., gray and white matter and soft tissues) without image artifact from bone, and it can differentiate between normal and pathologic tissue. MRI may be used to evaluate blood and cerebrospinal fluid flow, contraction and relaxation of organs such as the heart, and provide images of tissues in proximity to bone; because calcium does not interfere with MRI.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:868.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier, Churchill Livingstone; 2010:2466.

Rawson JV, Siegel MJ. Techniques and strategies in pediatric body MR imaging. *Magn Reson Imaging Clin N Am*. 1996;4:589.

A.3. What are some disadvantages associated with MRI? What are some safety concerns?

There are many hazards associated with an MRI suite. The constant static magnetic field, the pulsed (time-varied) gradient magnetic fields, and the high frequency RF waves all interact and when combined with a ferromagnetic object, can pose significant risk to the patient or operator. Not only can the attraction of these external objects become fatal, but implantable objects can dislodge and malfunction or burn

the patient. Depending on the distance from the core of the magnet, the magnetic field strength diminishes. Distances less than five gauss line can make pacemakers malfunction. Distances less than 50 gauss line can make ferromagnetic gas cylinders become lethal projectile missiles.

Obviously with the growing usage of implantable medical devices (i.e., pacemakers, vascular clips, automatic implantable cardioverter-defibrillators, mechanical heart valves, and implanted infusion pumps,) a potential exists for injury to the patients. Most anesthesiologists agree that magnetic resonance (MR) should not be conducted on patients with an implanted device, but that is not an absolute. Clips used in vascular surgery and neurosurgery need to be verified that they are nonferrous (e.g., titanium) to ensure immobility during the MR scan.

Owing to the potential for catastrophic events, recommendations for MRI safety have been proposed by the American College of Radiology. Briefly, the MRI suite should be separated into four zones: zone I is the public zone immediately outside the MRI suite, zone II is the reception area monitored by MRI personnel, zone III encompasses the control room with access to this area being restricted from the public, and zone IV is the physical MRI scanner room. Entry into zones III and IV should be screened by MRI personnel to ensure everyone's safety. Ferromagnetic objects should not be brought in to zone III but if necessary should be brought in with extreme caution. Items such as credit cards, pens, keys, laryngoscopes, scissors, stethoscopes, paper clips, ferromagnetic gas cylinders should be excluded from zone IV. At the author's institution, all oxygen E-gas cylinders have been replaced by aluminum cylinders to further ensure safety of our patients. Adherence to these zones must be maintained especially during emergent situations for the safety of the patient and personnel.

Safety terminology for devices and implants were devised by the U.S Food and Drug Administration, Center for Devices and Radiologic Health in 1997 to distinguish the safety of the device (MRI safe) and the compatibility of the device (i.e., the lack of artifacts on the exam) in a particular MR environment (MRI compatible). Over the years though, these labels were potentially being misused and due to safety concerns, a set of new terminologies were developed by the American Society for Testing and Materials International. *MR safe* refers to items with no known hazards in any MR environment. *MR conditional* refers to items that pose no known hazards in a specified MR environment (i.e., strength of the magnetic field). *MR unsafe* refers to items that pose definite hazards in all MR environments (i.e., ferromagnetic scissors). Concerns regarding the device and its potential hazards should be addressed by the staff members, on site radiologist, and/or manufacturer to determine whether the exam can be conducted in a safe manner.

Other disadvantages of the MRI include the potential for malfunction of electronic equipment (such as monitors and infusion pumps), as well as limited access to the patient. MRI safe/conditional monitors and machines should be used in the scanner. Thermal injuries have been reported from electrocardiogram (ECG) electrodes and pulse oximeter probes. All cables and monitoring equipments should be placed in a straight manner without coiling to ensure no such injuries. MRI safe/conditional infusion pumps can be used in zone IV, but otherwise pumps can be left in zone III and the tubing passed through a wave guide. The relatively long time necessary to obtain the images (as much as 15 minutes per image, with a total scanning period of 1 to 3 hours), and image degradation from any motion including cardiac contractions, respirations, cerebrospinal fluid flow, and bowel peristalsis are additional disadvantages. Another potential hazard to both the patients and the operators is the high decibels levels of sound emanating from the scanner due to the RF pulses (>90 dB). Hearing protection for both is manadatory even if the patient is under anesthesia. Due to the small bore of most MRI scanners (i.e., 50 to 60 cm in diameter), scanning obese patients may be impossible and a sense of claustrophobia and anxiety can be experienced.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:868.

De Andres J, Valia JC, et al. Magnetic resonance imaging in patients with spinal neurostimulation systems. *Anesthesiology*. 2007;106:779–786.

Kanal E, Borgstede JP, et al. American College of Radiology white paper on MR safety. *Am J Roentgenol*. 2002;178:1335–1347.

Levine GN, Gomes AS, et al. Safety of magnetic resonance imaging in patients with cardiovascular devices: an American Heart Association scientific statement from the committee in diagnostic and interventional cardiac catheterization, council on clinical cardiology, and the council on cardiovascular radiology and intervention. *Circulation*. 2007;116:2878–2891.

Menon DK, Peden CJ, Hall AS, et al. Magnetic resonance for the anaesthetist. Part I. Physical principles, applications, safety aspects. *Anaesthesia*. 1992;47:248.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier, Churchill Livingstone; 2010:2466–2468.

Patteson SK, Chesney JT. Anesthetic management for magnetic resonance imaging: problems and solutions. *Anesth Analg*. 1992;74:122.

Practice advisory on anesthetic care for magnetic resonance imaging: A report by the American Society of Anesthesiologists task force on anesthetic care for magnetic resonance imaging. *Anesthesiology*. 2009;110:459–479.

A.4. What are the contraindications to MRI?

Patients with implanted biologic devices, such as pacemakers, automatic implantable cardioverter-defibrillators, and certain pumps, should be excluded from MRI studies because of the possibility of device malfunction, inactivation, or damage in the magnetic field. In an MR environment, the device may be moved, rotated, dislodged or accelerated towards the magnetic core. In the case of certain metallic devices (i.e., leads) they can act as an "antenna" and concentrate the RF energy which can lead to thermal injuries. Fractured leads are absolutely contraindicated due to the high risk of thermal injuries. The safety of various cardiovascular devices for MR examination was reviewed based on ex vivo, animal and in vivo studies and reported by the American Heart Association (AHA) and has been found extremely helpful. Although many coronary stents, peripheral stents, sternal wires, inferior vena cava filters, prostethic heart valves, and annuloplasty rings have been deemed MR safe or conditional, it is important to review each type carefully and decide whether the proposed MR exam is in line with the specified milieu for the particular device. Currently, the American Heart Association and the American Society of Anesthesiologists (ASA) practice advisory task force on the anesthetic care for MRI regard the presence of a pacemaker or an implantable cardioverter-defibrillator (ICD) as a strong relative contraindication to routine MR examination. If the benefits far outweigh the risks of the exam, then the scanning should be performed in an experienced center with expertise in MR imaging and electrophysiology. The care of the patient should be performed in collaboration with the cardiologist, radiologist, device manufacturer, and the technician. Written consent must detail all risks to the patient including death. Full resuscitation equipment must be readily accessible in the MRI suite in case of an arrthymia or equipment malfunction. For a more thorough evaluation of these devices, please refer to the recommendations in the reference article. In contrary to these devices, some others may be better tolerated in the MRI suite. MRI may be performed on a limited basis for patients with certain deep brain stimulators and vagal nerve stimulators. Consultation with the radiologist, neurosurgeon, the referring physician, and perhaps the manufacturer, should be made to ensure the device is MRI safe/conditional for the particular protocol. Orthodontic braces and dentures and tattoos or cosmetics that contain metallic dyes, although safe, can degrade the image quality significantly.

Kanal E, Borgstede JP, Barkovich AJ, et al. American College of Radiology white paper on MR safety: 2004 update and revisions. *Am J Roentgenol*. 2004;182:1113.

Levine GN, Gomes AS, et al. Safety of magnetic resonance imaging in patients with cardiovascular devices: an American Heart Association scientific statement from the committee in diagnostic and interventional cardiac catheterization, council on clinical cardiology, and the council on cardiovascular radiology and intervention. *Circulation*. 2007;116:2878–2891.

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Practice advisory on anesthetic care for magnetic resonance imaging: A report by the American Society of Anesthesiologists task force on anesthetic care for magnetic resonance imaging. *Anesthesiology*. 2009;110:459–479.

A.5. What are the biologic effects of clinical MRI?

Although an area of controversy and ongoing investigation, most human data to date suggest that there are no significant deleterious effects to patients or health care professionals from exposure to the static magnetic field of an MRI. However, MRI capabilities were developed relatively recently (the 1960s), and epidemiologic evidence of harmful exposure may not yet be apparent. It seems prudent, therefore, to limit repetitive and readily avoidable exposure to the magnetic field. Also controversial is the use of MRI during pregnancy, as the effects of magnetic fields on the human fetus cannot be easily determined. However, current evidence does not support the suggestion that routine clinical exposure of the pregnant patient to MRI can cause developmental abnormalities in the fetus. Pregnant patients have undergone MRI safely during all stages of pregnancy. Nevertheless, caution is advised. Studies have shown that gadolinium-based contrast agents enter the fetal circulation and are filtered in the fetal kidneys into the amniotic fluid. It is unclear the duration of the substance in the fluid, but it can potentially form free gadolinium ions, which can theoretically pose risks to the developing fetus. The appropriateness of MRI examination and the acuteness of the diagnostic need must be considered. Ultrasonography use is preferred if it can provide equivalent diagnostic information, and consideration should be given to postponing the MRI until late in the pregnancy or until after delivery.

Colletti PM, Sylvestre PB. Magnetic resonance imaging in pregnancy. *Magn Reson Imaging Clin N Am*. 1994;2:291.

Kanal E, Borgstede JP, Barkovich AJ, et al. American College of Radiology white paper on MR safety: 2004 update and revisions. *Am J Roentgenol*. 2004;182:1113.

McBrien ME, Winder J, Smyth L. Anaesthesia for magnetic resonance imaging: a survey of current practice in the UK and Ireland. *Anaesthesia*. 2000;55:741–742.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier, Churchill Livingstone; 2010:2468.

A.6. What are the anesthetic considerations for this procedure?

The problems that complicate the anesthetic management of any patient outside the operating room environment exist for patients requiring sedation or general anesthesia for MRI. The MRI suite is often located some distance from the operating

room and the anesthesia department, thus limiting the availability of backup assistance and supplies. As with any remote anesthetizing location, the personnel may not be familiar with the requirements of anesthetized patients, thereby decreasing their ability to provide assistance. Frequently, the MRI suites have been designed without the consideration for anesthetic needs, such as pipeline gases, suction, or an anesthetic exhaust system. Access to a recovery suite for postanesthesia care may not be readily available, thereby necessitating a trip to the main recovery room.

In addition, there are anesthetic challenges unique to the MRI suite. Because of the bulkiness of the unit, the patient is often far removed from the anesthesiologist and access to the airway is limited. Intravenous lines, anesthesia circuits, oxygen tubings, and monitoring cables must be of sufficient length to reach the patient deep within the scanner. The strong magnetic field necessitates the exclusion of all ferromagnetic objects and equipment. The displays of standard monitoring devices can be distorted or displaced by the magnetic field and the monitors themselves can degrade the MRI image by disturbing the signal/noise ratio of the MRI. The ASA Task Force understands that the interpretation of the ECG may be limited due to the superimposed voltages from blood flow in a high magnetic field (i.e., ST-segment interpretation unreliable even with filters). Safe monitoring conditions must be maintained with MR safe/ conditional monitors, remote monitoring and remain in compliance with ASA standards.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:868.

Patteson SK, Chesney JT. Anesthetic management for magnetic resonance imaging: problems and solutions. *Anesth Analg*. 1992;74:123.

Practice advisory on anesthetic care for magnetic resonance imaging: A report by the American Society of Anesthesiologists task force on anesthetic care for magnetic resonance imaging. *Anesthesiology*. 2009; 110: 459–479.

Rogers MC, Tinker JH, Covino BG, eds. *Principles and Practice of Anesthesiology*. St. Louis: Mosby; 1993:2345.

A.7. What is intraoperative MRI?

Over the last decade, image-guided surgery systems have been introduced that combine the resources of an operating room with MRI technology and high-performance computing. Several low-, mid-, and high-field strength interventional magnetic resonance systems have been developed that permit access to the patient by surgeons and provide near–real-time imaging during surgical procedures. Intraoperative MRI (iMRI) furnishes the surgeon with the simultaneous combination of direct vision and beyond-the-surface MRI, allowing for more accurate localization and targeting during surgery. In addition, iMRI enables the surgeon to detect the full extent of lesions, to devise a surgical approach that is safe with less potential operative morbidity, and to monitor for unseen hemorrhage. Not surprisingly, iMRI systems are expensive and require the need for MRI-compatible surgical instruments and monitoring equipment. One of the largest challenges anesthesiologists face in this setting is dealing with the high energy iMRI generated electrical noise that can interefere with the ECG signal on the monitor. Unlike in an MRI suite, there are multiple people and objects to account for when the iMRI unit is brought out and engaged around the patient. During the duration of the scan, the anesthesiologist has no access to the patient and visualization of the patient may be limited when enclosed in an electrical noise shield. All ferromagnetic objects such as laryngoscopes, stylets, beepers must be left outside the operating room or placed in a secure area. Lastly, as opposed to an MR exam in a dedicated suite, the anesthetic considerations for iMRI must also include the needs of the ongoing complex surgical procedure.

Berkenstadt H, et al. Anesthesia for magnetic resonance guided neurosurgery. *J Neurosurg Anesthesiol*. 2001;13(2):161.

Dzwonczyk R, Fujii JT, et al. Electrical noise in the intraoperative magnetic resonance imaging setting. *Anesth Analg*. 2009;108:181–186.

Hall WA, et al. Intraoperative magnetic resonance imaging. *Top Magn Reson Imaging*. 2000;11(3):202–212.

Jolesz FA. Interventional and intraoperative MRI: a general overview of the field. *J Magn Reson Imaging*. 1998;8(1):5–6.

B. Preoperative Evaluation and Preparation

B.1. What type of patients may require sedation or general anesthesia for a magnetic resonance examination?

Although MRI is painless, patients must remain still throughout the time required to make each scan (as much as 15 minutes) to obtain images free of movement artifacts. Patients who are unable to cooperate adequately (e.g., infants, young children, and adults who are confused, mentally ill, intellectually subnormal) usually require an anesthesiologist to help reduce movement during the examination. Small infants may tolerate the procedure well if fed before the examination and swaddled in a blanket. Oral chloral hydrate is an excellent agent for sedation by nonanesthesiologists and is dosed 80 mg per kg to 100 mg per kg. Especially with computer tomography scans, chloral hydrate has been shown to be effective in children younger than 3 years. Side effects of this drug may include excessive sedation, agitation, or respiratory depression. Most children younger than 5 years of age and as old as 11 years of age require some form of sedation or general anesthesia. Not only are children needing anesthesia, but 30% of adult patients experience some form of anxiety during MR scanning. Anesthesiologists are frequently managing claustrophobic or anxious adults, as well as those requiring either airway protection (unconscious or critically ill patients) or mechanical ventilation (patients with head injuries or elevated intracranial pressure) to ensure that an adequate examination is obtained safely and efficiently.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:868.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier, Churchill Livingstone; 2010:2468–2469.

Peden CJ, Menon DK, Hall AS, et al. Magnetic resonance for the anaesthetist. Part II. Anaesthesia and monitoring in MR units. *Anaesthesia*. 1992;47:509.

Rogers MC, Tinker JH, Covino BG, et al., eds. *Principles and Practice of Anesthesiology*. St. Louis: Mosby; 1993:2345–2346.

B.2. What preoperative laboratory testing would you require for this patient?

For a routine MRI examination in this child, no preoperative laboratory tests would be required as long as anticonvulsant medications have been stable with documented adequate serum levels.

Cote CJ, Lerman J, Todres ID. *A Practice of Anesthesia for Infants and Children*, 4th ed. Philadelphia: Saunders Elsevier, 2009:527.

B.3. How would you premedicate this patient?

The goals of premedication for this child would be to provide anxiolysis and facilitate the induction of anesthesia without exacerbating a seizure. At the author's institution, ambulatory pediatric patients are not routinely given pharmacologic premedicants; rather, it is our practice to allow a parent to be present at the time of induction, in order to help allay the child's anxiety and ease the induction. If one elects to administer a sedative drug to this child, a logical choice would be oral midazolam (0.5 mg/kg, maximum 10 mg) in a small amount of cherry or strawberry syrup. It is also the practice at the author's institution that oral chloral hydrate is effective in children less than 12 months of age due to the longer duration of the MR scans in comparision to CT scans.

Cote CJ, Lerman J, Todres ID. *A Practice of Anesthesia for Infants and Children*, 4th ed. Philadelphia: Saunders Elsevier, 2009:506–7 and 513.

C. Intraoperative Management

C.1. What are some of the anesthetic options for this patient?

Many different anesthetic techniques have been used for anesthetizing children undergoing MRI or other painless radiologic procedures. These range from simple sedation with orally administered chloral hydrate, or rectally administered barbiturates, to intramuscularly administered meperidine/promethazine/Thorazine, to general anesthesia with ketamine, propofol, or inhaled anesthetics. Because conscious sedation of children is frequently insufficient to prevent patient movement, deeper levels of sedation or general anesthesia are required to successfully anesthetize the pediatric patient for MRI. The ideal anesthetic should allow the anesthesiologist the ability to titrate and maintain stable drug concentrations in order to prevent undesired patient movement during the scan and to provide rapid rates of induction and recovery with a minimal requirement for special MRI-compatible equipment.

Intravenous anesthesia with propofol meets several of the aforementioned criteria and is therefore an excellent technique for MRI. Continuous intravenous infusion of propofol allows for a precise, rapid titration to the desired effect and provides for a rapid recovery. Propofol use eliminates the need for a nonferromagnetic, MRI-compatible anesthesia machine and for a scavenger of waste anesthetic gases, both of which are the major drawbacks of an inhalational technique. Ketamine, although considered a potent bronchodilator with minimal respiratory depression, can increase salivation. This, especially in children, can cause upper airway obstruction, laryngospasm and microaspiration even in the presence of relatively intact upper airway reflexes. In addition, ketamine may elicit undesirable myoclonic movements, increased intracranial pressure, and emergence delirium.

Cote CJ, Lerman J, Todres ID. *A Practice of Anesthesia for Infants and Children*, 4th ed. Philadelphia: Saunders Elsevier, 2009:1001–1003.

Frankville DD, Spear RM, Dyck JB. The dose of propofol required to prevent children from moving during magnetic resonance imaging. *Anesthesiology*. 1993;79:953–958.

Martin LD, Pasternak R, Pudimat MA. Total intravenous anesthesia with propofol in pediatric patients outside the operating room. *Anesth Analg*. 1992;74:611.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier, Churchill Livingstone; 2010:2469.

C.2. How is an MRI conducted?

The patient is placed on a long, thin table outside the scanner. After obtaining an adequate level of anesthesia, the patient is positioned. If the head is to be examined, it is often enclosed within a small coil or tube. Next, the table with the patient is fed into the long tube of the MRI magnet. The portion of the body to be examined is usually centered in the magnet approximately 1 m from the end of the tube. During the examination, the delivery of the RF pulses produces a loud thumping noise, which can average 95 dB in a 1.5-T scanner. To obtain a high-quality scan, the patient must refrain from moving during the acquisition of an individual cut or from changing position at any time during the entire examination. An individual scan can take several minutes, and the total scanning time may be from 1 to 3 hours. Body surfaces can absorb some of the RF energy during the sequence but is unlikely to increase the patient's core temperature by more than one degree celsius. Nevertheless, the specific absorption rate of energy in the body as measured in watt per kilogram (W/kg) is monitored and depending on the patient, if too high, the sequence may need to be aborted and adjusted.

De Andres J, Valia JC, et al. Magnetic resonance imaging in patients with spinal neurostimulation systems. *Anesthesiology*. 2007;106:779–786.

Menon DK, Peden CJ, Hall AS, et al. Magnetic resonance for the anaesthetist. Part I. Physical principles, applications, safety aspects. *Anaesthesia*. 1992;47:246–247.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier, Churchill Livingstone; 2010:2467.

Peden CJ, Menon DK, Hall AS, et al. Magnetic resonance for the anaesthetist. Part II. Anaesthesia and monitoring in MR units. *Anaesthesia*. 1992;47:508.

C.3. How would you monitor this patient?

Reliable and accurate monitoring of an unconscious individual during an MRI is essential because the patient cannot be seen adequately nor easily accessed by the anesthesiologist. During sedation, the ASA standard monitors including blood pressure, pulse oximetry, and ECG need to be monitored. During general anesthesia, capnography and temperature should also be monitored. The assessment of ventilation in a spontaneously breathing patient may be difficult especially when the patient is within the magnet and far from view. Monitoring end-tidal carbon dioxide from one limb of the nasal oxygen prongs or through a nasal catheter is frequently successful. Monitoring pulse oximetry is a marker for oxygenation and should not be used as a marker for ventilation. Use of a precordial stethoscope may be unsatisfactory due to the length of tubing required and the loud noise of the MRI scanner. Hypothermia can be problematic, especially in the pediatric patient, because of the high airflow through the scanner cavity. The patient should be covered in blankets. Hyperthermia can also occur and if suspected based on specific absorption rate, the sequence may need to be temporarily stopped. Temperature monitoring can be accomplished by using nonferromagnetic temperature strips or probes with RF filters when feasible. It is currently not mandatory for the anesthesiologist to remain in the scanner room during the examination as long as remote monitoring with direct vision of the patient is possible.

Jorgensen NH, Messiak JM, Gray J, et al. ASA monitoring standards and magnetic resonance imaging. *Anesth Analg*. 1994;79:1141–1147.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier, Churchill Livingstone; 2010:2468–2469.

Peden CJ, Menon DK, Hall AS, et al. Magnetic resonance for the anaesthetist. Part II. Anaesthesia and monitoring in MR units. *Anaesthesia*. 1992;47:513–516.

Practice advisory on anesthetic care for magnetic resonance imaging: A report by the American Society of Anesthesiologists task force on anesthetic care for magnetic resonance imaging. *Anesthesiology*. 2009;110:459–479.

C.4. What special considerations apply to the monitoring equipment used during MRI?

Unshielded ferromagnetic materials within monitors and cables can interfere with imaging signals, causing a distortion of MRI results. Similarly, the radiofrequency RF signals of the scanner can induce currents in ferromagnetic elements of the monitors, causing a distortion of the monitoring signal, and making the monitor unusable. Fortunately, MR safe/conditional monitors and equipment (e.g., ECG electrodes) that use shielding nonferromagnetic components and filters to produce satisfactory functioning without a distortion of signal are readily available. Their use is preferred. In addition, to avoid magnetic pull, monitors should be placed at least 5 to 8 ft from the magnet bore or be permanently mounted.

The ECG may show significant changes within a static magnetic field. In particular the T waves and the late ST segments can mimic the ECG changes associated with conditions such as hyperkalemia and pericarditis. This is due to an induced voltage in blood (a conducting fluid) flowing through the magnetic field. These changes are directly related to field strength, but they do not appear to represent any significant physiologic alteration.

The high RF power used in MRI poses the risk of excessive heat at the monitoring sites and therefore the risk of thermal injury. To minimize the risk of burns from monitoring cables, one should do the following:

- Inspect the insulation on all monitoring wires to ensure that it is intact.
- Place cables and lead wires in straight alignment (do not allow monitoring wires to form loops).
- Remove all leads or wires not in use.
- Separate cables from patient's skin.
- Keep the cable and sensor out of the scanning area (e.g., place a pulse oximeter probe on the toe of a patient whose chest is being examined).
- Avoid excessive power.

Menon DK, Peden CJ, Hall AS, et al. Magnetic resonance for the anaesthetist. Part I. Physical principles, applications, safety aspects. *Anaesthesia*. 1992;47:249.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier, Churchill Livingstone; 2010:2467–2469.

Patteson SK, Chesney JT. Anesthetic management for magnetic resonance imaging: problems and solutions. *Anesth Analg*. 1992;74:122–123.

Peden CJ, Menon DK, Hall AS, et al. Magnetic resonance for the anaesthetist. Part II. Anaesthesia and monitoring in MR units. *Anaesthesia*. 1992;47:513–514.

C.5. How would you induce and maintain general anesthesia in this patient?

There are many different ways anesthesia can be induced in this child. Since this child does not have aspirational risk, inhalational induction can be performed safely. With a parent present, induction of anesthesia may be accomplished with an inhalation agent (e.g., sevoflurane) in nitrous oxide and oxygen through face mask in a room adjacent to the MRI scanner or at the greatest possible distance from the magnetic field within

the scanner room. After the child has lost consciousness, the parent is escorted back to the waiting room. Intravenous access is then established and all monitors are placed. The anesthetic level is deepened with a loading dose of propofol (e.g., 1 to 2 mg/kg), and if needed the airway is secured. Once the child is under general anesthesia, the child is then moved into the scanner room and placed on the MRI table. The patient and monitors are carefully positioned before attempting to advance the table into the magnet bore. Anesthesia is maintained with either a continuous intravenous infusion of propofol or inhalation agent, combined with nitrous oxide in oxygen.

Alternatively, an intravenous catheter may be inserted first and anesthesia induced with intravenous propofol 3 mg per kg or with any other intravenous induction agent.

Cote CJ, Lerman J, Todres ID. *A Practice of Anesthesia for Infants and Children*, 4th ed. Philadelphia: Saunders Elsevier, 2009:1001–1003.

Frankville DD, Spear RM, Dyck JB. The dose of propofol required to prevent children from moving during magnetic resonance imaging. *Anesthesiology*. 1993;79:954.

C.6. How would you maintain the airway during the scan?

Limited access to the patient's airway is one of the greatest challenges for the anesthesiologist during an MR scan. In light of this, it has been proposed by many, that securing the airway with either an endotracheal tube or laryngeal mask airway and ventilation be controlled, especially in those whose airway might potentially be problematic. Respiration can be spontaneous or controlled depending on personal preference and the needs of the patient. According to the ASA Task Force, the literature is silent in regards to the management of airway problems (i.e., obstruction, hypoventilation, larygnospasm) during an MR scan. As long as a plan is prepared should emergencies occur, any type of anesthetic can be used to accomplish the scan. Alternatively, total intravenous anesthestic with nasal cannula can be accomplished in lieu of an intubation. This should be considered in only patients with good natural airways whose ventilation is being monitored adequately. Placing a shoulder roll under the patient with the chin taped up may help prevent future airway obstruction during the MR scan. This should only be performed when there are no contraindications to potential spinal injuries with head and neck manipulations.

McBrien ME, Winder J, Smyth L. Anaesthesia for magnetic resonance imaging: a survey of current practice in the UK and Ireland. *Anaesthesia*. 2000;55:741–742.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier, Churchill Livingstone; 2010:2467–2469.

Peden CJ, Menon DK, Hall AS, et al. Magnetic resonance for the anaesthetist. Part II. Anaesthesia and monitoring in MR units. *Anaesthesia*. 1992;47:511.

Practice advisory on anesthetic care for magnetic resonance imaging: A report by the American Society of Anesthesiologists task force on anesthetic care for magnetic resonance imaging. *Anesthesiology*. 2009;110:459–479.

C.7. What is the laryngeal mask airway (LMA)?

The LMA is a device introduced by a British anesthesiologist, Dr. Archie Brain. It fills the gap in airway management between use of the face mask and tracheal intubation. Constructed of soft medical-grade silicone rubber, the LMA consists of an elliptical spoon-shaped mask with an inflatable rim fused at a 30-degree angle to an internally ridged tube with a standard 15-mm proximal connector. On the concavity of the laryngeal mask is a fenestrated aperture with three orifices through which

the distal end of the tube opens. The cuff of the mask is inflated through a pilot balloon. On the posterior curvature of the tube is a black line running longitudinally to assist in orientating the tube in situ. The standard LMA is latex free and contains no ferromagnetic components except a small metal spring in the pilot-tube valve mechanism. It is nondisposable, and can be autoclaved and reused numerous times (as many as 40). Alternatively, disposable LMAs are available which can be safely used as well.

The small amount of metal in the spring valve is not sufficient to be attracted by the magnetic field and dislodge the LMA. However, if the valve lies near the area being scanned, the scan's image can be distorted. There are flexible LMAs reinforced with a stainless steel wire coil, which should not be used during MRI.

In addition to these classic LMAs, there are a variety of other supraglottic airway devices which can be used in lieu of the classic LMA. Please refer to the individual device to determine whether or not ferromagnetic parts exist.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:757–761.

Brimacombe JR, Ferson D, Osborn I, et al. Specialized uses of the LMA. *Int Anesthesiol Clin*. 1998;36(2):130.

Landsman IS. The laryngeal mask airway. *Int Anesthesiol Clin*. 1997;35(3):50–51.

C.8. What are the advantages of the LMA compared with the face mask?

When used as an alternative to the face mask, the LMA gives the anesthesiologist more freedom to perform other tasks (e.g., record keeping, monitoring, and drug administration) and decreases the incidence of operator hand fatigue. The LMA allows for more reliable capnography and is capable of maintaining higher hemoglobin oxygen saturations. The contamination of the MRI scanner room environment with inhalational anesthetics is reduced and less manipulation of the airway is required with an LMA. Furthermore, injury to the eyes and facial nerves may be reduced by the avoidance of a face mask and head strap.

Boehringer LA, Bennie RE. Laryngeal mask airway and the pediatric patient. *Int Anesthesiol Clin*. 1998;36(2):45–60.

Brimacombe JR, Ferson D, Osborn I, et al. The laryngeal mask airway: limitations and controversies. *Int Anesthesiol Clin*. 1998;36(2):158.

Landsman IS. The laryngeal mask airway. *Int Anesthesiol Clin*. 1997;35(3):50–51.

Miller RD, ed. *Miller's Anesthesia*. 7th ed. Philadelphia: Elsevier, Churchill Livingstone; 2010:2468–2469.

C.9. What are the advantages of the LMA compared with the endotracheal tube (ETT)?

Although the LMA does not replace the ETT (especially in longer cases and when protection from aspiration is important), it has some advantages. The ease of LMA placement and provoking less stimulation (i.e., less coughing, gagging, swallowing, breath holding, bronchospasm, and cardiovascular response) are two advantages over the ETT. Lighter levels of anesthesia can therefore be better tolerated with an LMA than with an ETT. In inexperienced hands, the LMA can be more rapidly and reliably placed than an ETT, suggesting a potential role in resuscitation. Trauma to the vocal cords is limited because the LMA does not pass through this area. In adults, the incidence of sore throat after LMA usage is reduced when compared with the tracheal tube.

Brimacombe JR, Berry AM, White PF, et al. The laryngeal mask airway: limitations and controversies. *Int Anesthesiol Clin.* 1998;36(2):158.

Landsman IS. The laryngeal mask airway. *Int Anesthesiol Clin.* 1997;35(3):51–52.

C.10. What complications are associated with the use of the LMA?

The most serious potential problem of the LMA device is the lack of tracheal protection from aspiration of gastric contents. In patients at low risk of regurgitation, the rate of aspiration during general anesthesia using an LMA is similar to that in all non-LMA general anesthetics (2/10,000 cases). Most authors recommend that it not be used in patients at high risk of regurgitation. Conversely, aspiration of pharyngeal contents has not been shown to be a problem with the LMA, and the use of the device has been reported to be suitable during ear, nose, and throat procedures and dental procedures. Odynophagia occurs in 4% to 12% of patients after LMA use, an incidence that is comparable to the use of a face mask with an oropharyngeal airway. This is still less than that associated with tracheal intubation, which occurs in 30% of the patients. Hoarseness, dysphagia, and several cases of recurrent, hypoglossal and lingual nerve injury have been reported with LMA use. Cuff overinflation, unmonitored increases in cuff pressure secondary to nitrous oxide diffusion, light anesthesia with constriction of pharyngeal musculature, venous engorgement and tissue edema associated with the head-down position, and lidocaine gel lubricant have all been cited as causes of nerve injury. One fatal case has been implicated with the use of an intubating LMA. An unrecognized esophageal tear from an accidental blind esophageal intubation resulted in septic shock and death 9 weeks postintubation. Although this complication was a result of the blind intubation, it nevertheless was associated with an LMA device.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia.* 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:760.

Brimacombe JR, Berry AM, White PF. The laryngeal mask airway: limitations and controversies. *Int Anesthesiol Clin.* 1998;36(2):159.

Landsman IS. The laryngeal mask airway. *Int Anesthesiol Clin.* 1997;35(3):51.

C.11. What are contraindications to the use of the LMA?

The following conditions contraindicate the use of the LMA:

- Increased risk of gastric regurgitation (i.e., full stomach, hiatal hernia, bowel obstrucion, delayed gastric emptying)
- Limited ability to open the mouth or extend the neck (e.g., severe rheumatoid arthritis and ankylosing spondylitis), making advancement of the LMA into the hypopharynx difficult
- Low pulmonary compliance or high airway resistance
- Airway obstruction at or below the level of the larynx
- Oropharyngeal pathology (e.g., hematoma, abscess, and tissue disruption)
- Single-lung ventilation

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia.* 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:760.

Landsman IS. The laryngeal mask airway. *Int Anesthesiol Clin.* 1997;35(3):52–53.

Pennant JH. The laryngeal mask airway. Its uses in anesthesiology. *Anesthesiology.* 1993;79:158–159.

C.12. What are indications for the use of the LMA?

The LMA is best suited for use in any patient in whom anesthesia can be safely maintained through a face mask (except in a patient with oropharynx pathology). It has been used routinely in various surgical procedures including minor gynecologic, urologic, orthopedic, bronchoscopic, and endoscopic diagnostic procedures. In addition, the device may be useful in surgery around the face in which the trachea is intubated solely due to the physical interference imposed by the face mask. Other types of surgery in which the LMA has been used successfully include dental extraction, adenotonsillectomy, repair of cleft palate, myringotomy and placement of tympanostomy tubes, and eye surgery. Furthermore, use of the LMA in the management of the difficult airway is increasing.

Asai T, Morris S. The laryngeal mask airway: its features, effects and role. *Can J Anaesth*. 1994;41:944–945.

Nair I, Bailey PM. Review of uses of the laryngeal mask in ENT anaesthesia. *Anaesthesia*. 1995;50:898–899.

C.13. What size LMA is appropriate for this child, and how much air would routinely be required to properly inflate the cuff?

In this 15-kg patient, a size 2.0 LMA with a cuff volume of 5 to 10 mL would be appropriate. A guide to selecting the appropriate LMA based on patient weight, as well as the cuff volumes of the different LMAs, is shown in Table 61.1.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:758.

Boehringer LA, Bennie RE. Laryngeal mask airway and the pediatric patient. *Int Anesthesiol Clin*. 1998;36(2):48.

C.14. How is the LMA prepared?

Before insertion, the cuff of the LMA should be carefully inspected, tested for leaks, completely deflated, and lubricated. Only nonsilicone, water-based gels are used for

Table 61.1 The Selection of Laryngeal Mask Airway Size and Cuff Volume According to Patient's Weight

LARYNGEAL MASK AIRWAY SIZE	PATIENT WEIGHT (kg)	MAXIMUM CUFF VOLUME (mL)
1	<5	4
1.5	5–10	7
2	10–20	10
2.5	20–30	14
3	30–50	20
4	50–70	30
5	>70	40

lubrication and are applied only to the posterior surface of the mask. Care should be taken to avoid lubricating the anterior surface because the lubricant may obstruct the distal aperture or be accidentally aspirated into the larynx. Lubricants containing local anesthetics have been implicated in postoperative numbness, allergic reactions, and nerve damage and are not recommended for use with the LMA.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:758–759.

Brimacombe JR, Berry AM, White PF. The laryngeal mask airway: limitations and controversies. *Int Anesthesiol Clin*. 1998;2(36):159.

Ferson DZ. Laryngeal mask airway: preanesthetic evaluation and insertion techniques in adults. *Int Anesthesiol Clin*. 1998;2(36):33–34.

Landsman IS. The laryngeal mask airway. *Int Anesthesiol Clin*. 1997;35(3):55–56.

C.15. How is the LMA inserted?

According to the insertion technique described by the device's inventor, Dr. Brain, the operator places his nondominant hand under the patient's occiput and extends the patient's head at the atlantooccipital joint after induction of general anesthesia. This maneuver tends to open the mouth. The device, which has been lubricated and deflated appropriately, should be held like a pen with the index finger of the dominant hand positioned at the junction of the tube and the mask. It is firmly applied against the hard palate as the LMA is guided over the back of the tongue. Force is applied by the index finger in an upward direction toward the top of the patient's head as the device is directed along the palate and slid into the pharynx and hypopharynx, until the resistance of the upper esophageal sphincter is felt. The LMA is then stabilized with the nondominant hand as the inserting hand is removed from the patient's mouth. The cuff is then inflated with just enough air to form an effective seal. One should be able to observe a rising of the cricoid and thyroid cartilages and the lifting of the tube out of the mouth as the cuff is inflated. The longitudinal black line on the surface of the tube is oriented superiorly and should lie against the upper lip in the midline. Tape is used to secure the LMA in position in a manner similar to that used to secure an ETT. A major pitfall in the placement of the LMA is when posteriorly directed pressure is applied, resulting in the tip to be malpositioned, which can lead to trauma and a leak. A bite block may be inserted between the teeth to prevent biting and occlusion of the LMA barrel.

When correctly positioned, the bowl of the LMA mask lies over the laryngeal inlet with the tip of the LMA cuff resting against the upper esophageal sphincter in the hypopharynx, and the sides of the cuff resting in the pyriform fossae. Although the epiglottis often lies within the bowl of the LMA mask, the device usually creates a satisfactory airway even when the epiglottis assumes an awkward position (e.g., downfolded).

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:758–759.

Ferson DZ. Laryngeal mask airway: preanesthetic evaluation and insertion techniques in adults. *Int Anesthesiol Clin*. 1998;2(36):34–35.

C.16. What additional maneuvers may be attempted if difficulty is encountered when inserting the LMA?

For the experienced user, the standard insertion technique is successful in most patients (>98%) on the first two attempts. Common reasons for difficult insertion include poor

technique, inadequate depth of anesthesia (with resulting cough, retching, and laryngospasm), user inexperience, inability to negotiate the 90-degree turn from the posterior pharynx to the hypopharynx, a large tongue or tonsils, and use of an incorrectly sized LMA. Numerous maneuvers have been described to overcome insertion difficulties, including physically pulling the tongue forward, thrusting the jaw, and using a laryngoscope, a tongue blade, or a Magill forceps to lift the tongue. Inserting the LMA with the mask facing backward and rotating the device 180 degrees after meeting posterior pharyngeal wall resistance has also been advocated. Partially or completely inflating the cuff before insertion has been suggested to ease insertion. Although this maneuver may offer some advantages for an inexperienced user, it has the potential to cause partial airway obstruction if the tip of the LMA travels in front of the arytenoids toward the larynx. Furthermore, it may increase coughing or laryngospasm because of stimulation of protective airway reflexes or result in a high LMA position in the pharynx. In the patient with a high arched palate, approaching the hard palate slightly diagonally from the side with the LMA situated 15 to 20 degrees lateral from the midline may be useful.

Barash PG, Cullen BF, Stoelting RK eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:758–759.

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Ferson DZ. Laryngeal mask airway: preanesthetic evaluation and insertion techniques in adults. *Int Anesthesiol Clin*. 1998;2(36):35–42.

Landsman IS. The laryngeal mask airway. *Int Anesthesiol Clin*. 1997;35(3):55–56.

C.17. Examination of the patient before the table is fed into the MRI scanner reveals wheezing. What most likely is happening, and what do you do?

Wheezing in the setting of an LMA can be caused by light anesthesia resulting in partial laryngospasm, bronchospasm, or malposition of the device with the tip of the mask encroaching on the glottis. One should deepen the anesthetic in the spontaneously breathing patient or administer muscle relaxant in the mechanically ventilated patient as an initial treatment. If the problem is not relieved, despite an adequate level of anesthesia and/or paralysis, the device should be removed and repositioned.

Brimacombe JR. Problems with the laryngeal mask airway: prevention and management. *Int Anesthesiol Clin*. 1998;36(2):141.

C.18. Discuss how the LMA can be used as a conduit for tracheal intubation.

Outside of the zone IV MRI suite, the LMA has been used successfully as a conduit for blind tracheal intubation with an ETT, intubating tracheal stylet or fiber-optic bronchoscope (FOB)–guided ETT. Blind techniques at intubation through the LMA have the greatest chance of success when the LMA has a perfect central position around the larynx (45% to 60%) versus a noncentral location. The ability to effectively pass an ETT blindly through the LMA into the trachea can be further enhanced with the use of concomitant cricoid pressure. With any blind technique, care must be taken because laryngopharyngeal injury can result.

As opposed to these aforementioned blind techniques, the passage of an FOB through the LMA is approximately 100% successful and often less traumatizing.

Table 61.2 The Laryngeal Mask Airway Size That Can Accommodate the Size of Endotracheal Tube and Fiber-optic Bronchoscope

LARYNGEAL MASK AIRWAY SIZE	LARGEST ENDOTRACHEAL TUBE (ID, MM)	FIBER-OPTIC BRONCHOSCOPE SIZE (MM)
1	3.5	2.7
2	4.5	3.5
2.5	5.0	4.0
3	6.0 cuffed	5.0
4	6.0 cuffed	5.0
5	7.0 cuffed	6.0

With an appropriately sized ETT (see later discussion) threaded on the proximal end of the FOB, the scope is passed through the lumen of the LMA and under direct visualization into the trachea. The ETT is then passed over the shaft of the FOB and into the trachea. Unfortunately there are three major disadvantages associated with this technique. First, the ETT needs to be long enough to ensure that the cuff is situated below the vocal cords when the LMA is left in situ, especially in patients with long incisor-to-glottis distances. Second, the internal diameter of the LMA limits the size of the ETT that can be used, which can potentially hinder one's ability to provide effective ventilation. Third, the removal of the LMA over the ETT may risk extubation, which may be difficult to replace. Various solutions to these problems have been proposed, including the use of a tube exchanger to replace the LMA and ETT or deflating the LMA cuff to gain another 1.0 to 1.5 cm of depth in which to advance the LMA and ETT together. However, if the ETT that has been passed through the LMA is of adequate size, the LMA should be left in place with its cuff deflated. Table 61.2 lists the LMA size that can accommodate the size of ETT and FOB.

In addition, a specialized LMA designed to provide a superior conduit for blind or fiber-optically guided tracheal intubations was introduced into clinical practice in 1997. The intubating LMA (LMA-Fastrach) permits single-handed insertion from any position without moving the head and neck from a neutral position and without placing the operator's fingers in the patient's mouth. It consists of an anatomically curved, rigid airway tube constructed of stainless steel and covered with a rubberized material that is wide enough to accept an 8-mm cuffed ETT and is short enough to ensure passage of the ETT cuff beyond the level of the vocal cords. A rigid handle is attached to the distal end of the airway tube to facilitate one-handed insertion, removal, and adjustment of the device's position. The mask aperture bars found on the standard LMA are replaced by a hinged epiglottic elevating bar on the LMA-Fastrach. During intubation with the LMA-Fastrach, the epiglottic elevating bar serves to lift the epiglottis as the ETT emerges from the mask aperture, providing the ETT with an unobstructed path through the vocal cords into the trachea. A special 8-mm, straight, silicone, wire-reinforced ETT is available and should be used for intubation through the LMA-Fastrach, rather than with a standard plastic ETT, to decrease the likelihood of laryngeal trauma.

Barash PG, Cullen BF, Stoelting RK eds. *Clinical Anesthesia.* 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:767–768.

Campo SL, Denman WT. The laryngeal mask airway: its role in the difficult airway. *Int Anesthesiol Clin.* 2000;38(3):34–38.

Ferson DZ, Brimacombe J, Brain AI, et al. The intubating laryngeal mask airway. *Int Anesthesiol Clin.* 1998;36(2):185–189.

Landsman IS. The laryngeal mask airway. *Int Anesthesiol Clin.* 1997;35(3):52–59.

C.19. Discuss the uses of the LMA in the patient with a difficult airway.

In addition to serving as a routine airway during general anesthesia, the LMA has proved to be valuable in supporting airways that are difficult to manage and useful as a conduit for tracheal intubation. Uses of the LMA in the patient with a difficult airway include the following:

- *As a conduit for fiber-optic tracheal intubation in the awake patient*. When the preoperative evaluation indicates that the patient should be tracheally intubated awake, the LMA can be placed in the properly prepared awake patient and used as a conduit for fiber-optic intubation. Insertion of an LMA is a relatively moderate stimulus that may be better tolerated by the awake patient than the very stimulating methods of conventional rigid laryngoscopy and bronchoscopy. Visualization of the laryngeal inlet with an FOB is usually easy through the shaft of a properly positioned LMA. In patients whose airways are potentially difficult but who do not require endotracheal intubation, an LMA can be placed when they are awake and used as the primary means of airway control.
- *As an airway in the anesthetized patient who cannot be tracheally intubated*. The LMA is an alternative to the face mask in the patient under general anesthesia who cannot be tracheally intubated but whose lungs can be ventilated using a mask. An exception to this is the patient in whom cricoid pressure must be continuously applied (e.g., the patient at risk of regurgitation). In this situation, placement of the LMA does not protect the airway from regurgitation and would have little benefit over a conventional mask. As noted in section C.8, the LMA has several advantages over the face mask. An additional advantage of the LMA is that it can be used as a conduit for FOB intubation.
- *As a conduit for FOB tracheal intubation in the anesthetized patient who cannot be intubated, but whose lungs can be ventilated.* Refer to section C.18.
- *As an emergency airway in the patient who cannot be ventilated or intubated*. Insertion of the LMA has provided a life-saving emergency airway in this situation and is a reasonable maneuver to try before the tracheal esophageal Combitube or transtracheal jet ventilation, provided that there is no known periglottic pathology. The LMA works well as a routine airway device in most patients, and it is usually easily placed in patients whose airways are Mallampati class 3 or 4 and/or grade III or IV laryngoscopic view. Most anesthesiologists are familiar with the placement of an LMA and can effectively insert one with little trauma.
- *As a conduit for tracheal intubation in the patient who cannot be ventilated or intubated*. If the airway is successfully established with an LMA in this situation, precious time has been obtained to subsequently use the LMA as a conduit for tracheal intubation. If the LMA provides for adequate ventilation, it is likely that the glottic opening lies within the bowl of the LMA, and FOB-guided intubation through the LMA will be successful. If ventilation is poor after LMA insertion, the LMA may not be adequately aligned with the laryngeal inlet or there may be periglottic pathology. In both situations, FOB-guided tracheal intubation may be difficult and may necessitate insertion of a tracheal esophageal Combitube, initiation of transtracheal jet ventilation, or creation of a surgical airway.

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D. Postoperative Management

D.1. When is the LMA removed?

The removal of an LMA during excitation stages of emergence may cause coughing and/or laryngospasm; therefore, it should be removed either when the patient is deeply anesthetized or awake. Suctioning of secretions from the pharynx is usually not necessary before removal of the LMA. If suctioning is to be performed, it is important to ensure that an adequate level of anesthesia is maintained to avoid unnecessary airway stimulation. The cuff of the LMA may be deflated before removal or alternatively it may be left fully inflated to scoop out the secretions collected above the mask as it is withdrawn. As with extubation of the trachea, equipment for managing airway emergencies must be immediately available.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:760.

D.2. How will you have the patient recover from anesthesia?

Postanesthesia recovery care after an MRI is the same as that required after an anesthetic in the operating room. This can be accomplished in a designated area of the MRI suite provided that adequate facilities and trained personnel are available. For most, such a facility may not be available and the patient will require transport to the main recovery room. To transport the patient quickly and safely, one must ensure that adequate personnel and the proper equipment are organized in advance. It is useful to have the location of recovery and logistics of transport (if necessary) planned before the procedure begins.

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CHAPTER 62

Morbid Obesity and Obstructive Sleep Apnea

Jon D. Samuels and Fun-Sun F. Yao

A 46-YEAR-OLD WOMAN

was scheduled for elective laparoscopic sleeve gastrectomy. She had a past medical history significant for morbid obesity (MO) (height, 5 ft 4 in.; weight, 176 kg; body mass index [BMI], 66.6 kg per m^2), Pickwickian habitus, mild rheumatoid arthritis, osteoarthritis, mild asthma, hypertension, adult-onset diabetes mellitus, peptic ulcer disease with severe gastroesophageal reflux, and obstructive sleep apnea (OSA). She experienced daytime somnolence, heavy nighttime snoring, and had slept in a seated position for the previous 2 years. She was able to walk around the house with a cane, but was unable to climb any stairs. A preoperative diagnostic polysomnogram (PSG) was performed, and an apnea–hypopnea index (AHI) of 42 was calculated. Two weeks before surgery, home oxygen therapy with bilevel positive airway pressure (BIPAP) settings had been started at the following settings, with symptomatic improvement: FIO_2 of 0.35, respiratory rate 10 breaths per minute, inspired positive airway pressure of +11 cm H_2O, expired positive airway pressure of +4 cm H_2O, spontaneous mode. Cardiology clearance was obtained as a high-risk candidate, after an echocardiogram revealed mild right-sided cardiomegaly and mild pulmonary hypertension. The patient's blood pressure was 155/82 mm Hg, pulse was 60 beats per minute, and respiration was 20 breaths per minute.

A. Medical Disease and Differential Diagnosis

1. What problems exist with this patient?
2. Define the terms overweight, obesity, MO, super obesity (SO), normal weight, and ideal body weight (IBW). What is the BMI, and how is it measured?
3. What is OSA? What is the significance of OSA in the surgical population? What are the risk factors for OSA?

4. How is OSA diagnosed? Are there any validated questionnaires that have been endorsed by the American Society of Anesthesiologists (ASA)? Are any commonly observed physical findings associated with OSA? What is a sleep study or PSG? How are results obtained from a PSG used to grade the severity of OSA? What are the criteria for ordering a preoperative screening PSG?
5. What are the different types of OSA?
6. What is the Pickwickian syndrome (PS)? What is the pathogenesis of severe OSA?
7. What is the association between obesity and OSA? What is the etiology of pharyngeal pathology in severe obesity? Are all of the changes in the airway confined to the upper airway in obese patients with OSA?
8. What are the anesthetic implications of OSA?
9. What kind of metabolic problems would you expect to find in morbidly obese patients?
10. Describe the changes that occur in the following respiratory parameters in morbidly obese patients:
    - *Pulmonary mechanics:* tidal volume (V_T), functional residual capacity (FRC), residual volume (RV), vital capacity (VC), inspiratory reserve volume (IRV), expiratory reserve volume (ERV), and total lung capacity (TLC)
    - Flow volume loops
    - Pressure volume loops
    - Diffusing capacity for carbon monoxide (DLCO)
    - *Compliances:* lung, chest wall, and total
    - *Resistance:* airway, and total respiratory system
    - Closing capacity
    - Work of breathing
11. What changes occur in Pa_{O_2} and Pa_{CO_2} in morbidly obese patients?
12. What changes occur in intrapulmonary shunt (Q_S/Q_T) and dead space (V_D/V_T) in morbidly obese patients? Describe the equations.
13. What is the impact of pneumoperitoneum (PNP) on the respiratory and cardiovascular system of the bariatric surgical patient? Are there any other effects?
14. What changes occur in the cardiovascular system of the obese patient? Discuss cardiac output (CO), blood volume, blood pressure, and pulmonary arterial pressure.
15. Are there any other disease entities commonly associated with obesity?
16. What anatomic changes that affect the airway are associated with MO?
17. What derangements of the gastrointestinal system are associated with MO?

B. Preoperative Evaluation and Preparation

1. How would you evaluate this patient preoperatively?
2. Interpret the following arterial blood gases: pH 7.25; Pa_{CO_2} 50 mm Hg; Pa_{O_2} 58 mm Hg; and HCO_3^- 25 mEq/L on room air.
3. What is the equation for blood pH?
4. What are the normal values for blood pK_a, dCO_2, HCO_3^-, and H_2CO_3?
5. Interpret the following spirometry screening test: VC 2.36 L (expected 3.375 L); forced expiratory volume in 1 second (FEV_1) per forced vital capacity (FVC) 82%; and VC 70% of expected value.

6. How would you premedicate this patient? Why?
7. Describe weight-based dosing.

C. Intraoperative Management

1. How would you monitor this patient?
2. The ASA's Difficult Airway Algorithm provides a guideline for management of the difficult airway. How do the comorbidities of MO and OSA modify implementation of the algorithm?
3. How would you induce anesthesia? Describe the intubation technique.
4. Why is it important to preoxygenate the obese patient? How would you do it? Compare the effectiveness of the four-maximum-breath and 3-minute techniques.
5. There are many new airway devices on the marketplace. Which of these devices have been particularly successful on the morbidly obese or OSA patient?
6. How would you maintain general anesthesia? What agents would you choose?
7. Which muscle relaxants would you use?
8. Can regional anesthesia be used intraoperatively and postoperatively to decrease opioid requirements? What are the advantages and disadvantages of regional anesthesia? What are some of the newer techniques available?
9. What is the effect of narcotics on the sphincter of Oddi? Is pharmacologic treatment indicated?
10. During surgery, arterial blood gases showed pH 7.35; Pa_{O_2}, 57 mm Hg; Pa_{CO_2}, 52 mm Hg; F_{IO_2}, 0.6; mechanical ventilator V_T, 1.0 L; and ventilatory rate, 15 breaths per minute. The following changes were made to the ventilatory parameters: 10 cm H_2O positive end-expiratory pressure (PEEP) was added, and the V_T was increased to 1.2 L. Twenty minutes later, an arterial blood gas showed pH 7.32; Pa_{O_2}, 55 mm Hg; and Pa_{CO_2}, 55 mm Hg. What is the explanation for these changes?
11. What is apneic oxygenation? Who did the pioneer study?
12. What is diffusion hypoxia? How do you prevent it?

D. Postoperative Management

1. When will you extubate this patient? What are the extubation criteria?
2. What are the major early postoperative complications in the morbidly obese patient? How do health-related risks correlate with obesity? What factors correlated statistically with perioperative mortality?
3. How does position affect respiratory function in the obese patient?
4. How would you prevent postoperative atelectasis?
5. How long would you prescribe supplementary oxygen postoperatively?
6. How would you control postoperative pain?

A. Medical Disease and Differential Diagnosis

A.1. What problems exist with this patient?

Preoperative significant past medical history in this patient consists of MO, OSA, possible PS, right ventricular hypertrophy, mild pulmonary hypertension, systemic hypertension, adult-onset diabetes mellitus, osteoarthritis, mild rheumatoid arthritis, and severe gastroesophageal reflux disease. Epidemiologically, this patient is at increased

risk for coronary artery disease, cardiac arrhythmias, left- and right-sided congestive heart failure, peripheral vascular disease, venous thrombosis and pulmonary emboli, cerebrovascular disease, biliohepatic disease, hepatic steatosis, hepatic cirrhosis, degenerative joint disease, and socioeconomic and psychosocial impairment.

This is a high-risk patient, with increased risk of both perioperative morbidity and mortality. Major anesthetic concerns include risk of difficult airway, DMV, decreased apneic threshold to trace amount of anesthetics, sedatives and narcotics, prolonged anesthesia emergence, postemergence resedation, positional ventilatory collapse, restrictive and obstructive lung disease, ventilation–perfusion mismatch, and worsening of reactive pulmonary hypertension and cor pulmonale. This patient must receive continuation of her preoperative oxygen therapy with continuous positive airway pressure (CPAP) in the immediate recovery period, at the values determined by her sleep study (PSG), or greater. Minor anesthetic concerns include difficult monitoring, difficult vascular access, and positioning issues. Additionally, there is a rare risk of postoperative massive pharyngeal collapse, rhabdomyomysis with renal failure, increased risk of infection including pneumonia, positional injuries. Meticulous attention to acute pain management is essential.

Safe perioperative care for this patient requires triage to a specialized facility, additional personnel, surgeons with advanced laparoscopic training, and anesthesiologists with advanced airway skills and optimal equipment.

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A.2. Define the terms overweight, obesity, MO, super obesity (SO), normal weight, and ideal body weight (IBW). What is the BMI, and how is it measured?

Obesity is a multifactorial chronic disease involving social, cultural, physiologic, psychologic, metabolic, endocrine, genetic, and behavioral components, resulting in excess adipose and tissue mass. The modern basis for the determination of demographics is the BMI, or Quetelet's Index, after the Belgian statistician, Adolphe Quetelet, published in 1842, and is measured in body weight in kilograms divided by the height in meters squared (kg per m^2). The standard for IBW, the sex-specific desirable weight for persons with small, middle, and large frames, is published in the Metropolitan Life insurance tables.

- *Anorexia* is defined as a BMI of less than 17.5 in men or women.
- *Underweight* is defined as a BMI of 17.6 to 19.0 in women, or 17.6 to 20.6 in men.
- *Ideal (normal) weight* is defined as a BMI of 19.1 to 25.8 in women, and 20.7 to 26.4 in men.

- *Marginally overweight* is defined as a BMI of 25.9 to 27.2 in women, and 26.5 to 27.8 in men.
- *Overweight* is defined as a BMI of 27.3 to 32.3 in women, and 27.9 to 31.1 in men.
- *Obesity* is defined as a BMI of 32.4 to 34.9 in women, and 31.2 to 34.9 in men.
- *Severe obesity* is defined as a BMI of 35.0 to 39.9 in both sexes.
- *Morbid Obesity* is defined as a BMI of greater than 40.
- *Super Obesity*, a relatively new term, is defined as a BMI greater than 50.

There exist imperial and metric system BMI tables and web-based calculators.

Occasionally, an approximate, non–sex-specific system is used. In this system, a *healthy* (*normal*) *weight* is a BMI of 18.6 to 24.9, *overweight* is a BMI of 25 to 29.9, *obesity* is a BMI of 30 to 34.9, *severe obesity* is a BMI of 35 to 39.9, *MO* is a BMI of more than 40.0.

The older definitions of obesity may occasionally suffice. Overweight was formerly defined as a body weight of up to 20% greater than the predicted ideal weight, and obesity of more than 20%. MO was formerly defined as a body weight of 100 lb above the IBW, or alternatively, of twice the IBW. These definitions involved value judgments and inaccuracies, and were later abandoned, in favor of more objective terminology.

Alternative systems for the determination of obesity exist. In the triceps skinfold thickness test, for example, obesity is defined as a value of greater than 23 mm in men or greater than 30 mm in women. In the Broca Index (height in centimeters minus 100 for men and minus 105 forwomen), the IBW is calculated in kilograms.

- *Men*: ideal body weight (kg) = height (cm) – 100
- *Women*: ideal body weight (kg) = height (cm) – 105

There are different patterns of distribution of obesity. In *peripheral obesity* (e.g., gynoid or gluteal pattern), the individual has a pear shape, and adipose tissue deposition is predominantly in the lower body. In *central obesity* (e.g., android, or cushingoid), and especially upper body obesity, the individual has an apple shape, and adipose tissue deposition occurs predominantly in the upper body. Central obesity has greater associations with perioperative risk and OSA.

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A.3. What is OSA? What is the significance of OSA in the surgical population? What are the risk factors for OSA?

OSA is a sleep disorder. Sleep disorders may be grouped into the following types: conditions with excessive daytime somnolence (e.g., OSA), conditions with disorders initiating and maintaining sleep (e.g., insomnia), and circadian rhythm disorders (e.g., jet lag).

In the older terminology, OSA referred to both OSA proper, and to obstructive sleep hypopnea (OSH) syndrome, a milder variant. Currently, it is more precise to refer to obstructive sleep apnea and hypopnea syndrome (OSAHS) when naming the general condition. OSA is the most prevalent sleep disorder, affecting 2% to 26% of the general population. OSA is a major risk factor for perioperative adverse events, as shown in the literature. The prevalence of OSA is higher in the surgical population than in the general population. It is estimated that 70% of the bariatric surgical candidates have moderate-to-severe OSA. In most cases, there is no screening, and diagnosis preoperatively.

OSA is defined as cessation of airflow for more than 10 seconds despite continuing ventilatory effort, five or more times per hour of sleep, associated with a decrease in arterial oxygen saturation (Spo_2) of greater than 4%. *OSH* is defined as a decrease in airflow of more than 50% for more than 10 seconds, 15 or more times per hour of sleep, associated with a decrease in Spo_2 of greater than 4%. Both forms of OSAHS are usually associated with snoring, sleep disruption from increased ventilatory effort–induced arousal, hypersomnolence (daytime sleepiness), altered cardiovascular function, and pathophysiologic alterations, of which hypoxemia and hypercarbia are primary events, and polycythemia, systemic and pulmonary hypertension, various cardiac arrhythmias, myocardial ischemia, right and left ventricular hypertrophy, and eventually, failure are secondary events.

Severe obesity is an independent risk factor for OSAHS. However, not all forms of obesity are linked to OSA. Peripheral obesity and gynecoid obesity have little association with OSA. Central obesity, on the other hand, is associated with OSA, particularly in patients who possess an increased waist circumference or increased neck circumference. Of all risk factors, the strongest correlation is with waist circumference, in particular if the waist-to-hip ratio was >1 in men and >0.85 in women. Craniofacial markers for OSA include increased neck circumference, jowls, poor Mallampati class (3 or 4), and short cricomental space (defined as the perpendicular distance from the cricoid cartilage to the inner mentum of the skin of the neck). In nonobese individuals, risk factors are craniofacial dysostoses, particularly micrognathia (absolute or relative), cartilaginous abnormalities (e.g., lingual tonsillar hyperplasia), chronic nasal obstruction, and tonsillar hypertrophy. Other risk factors include male gender, middle age, evening ingestion of alcohol, and drug-induced sleep.

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A.4. How is OSA diagnosed? Are there any validated questionnaires that have been endorsed by the American Society of Anesthesiologists (ASA)? Are any commonly observed physical findings associated with OSA? What is a sleep study or PSG? How are results obtained from a PSG used to grade the severity of OSA? What are the criteria for ordering a preoperative screening PSG?

OSA may be suspected by history, physical examination, or comorbidities, but definitive diagnosis requires a sleep study.

A concise and easy-to-use screening tool for OSA has been developed and validated at preoperative clinics. The STOP questionnaire, stands for habitual Snoring, Tiredness or daytime sleepiness, Observed apnea, and high blood Pressure. When combined with BMI, age, gender, and neck size, the STOP questionnaire has a high sensitivity, especially for moderate to severe OSA. The Berlin questionnaire, which is commonly utilized in preoperative clinics, also efficiently screen for OSA.

Most adults with OSA have upper body obesity, increased neck circumference, micrognathia, and poor Mallampati scores on physical examination. Patient characteristics typically associated with OSA are a higher BMI, hypertension, and certain cephalometric measurements. In 90% of cases, the patient has a BMI in excess of 28 kg per m^2. OSA, however, may result from any condition that predisposes to upper airway obstruction. Some examples are pregnancy, upper airway abnormalities (e.g., deviated nasal septum, hypertrophic tonsils, and adenoids), cartilaginous abnormalities (e.g., lingual tonsillar hyperplasia), craniofacial dysostoses, and certain congenital conditions (e.g., Down syndrome, muscular dystrophy). The absence of a typical or compelling presentation, however, does not rule out the possibility of OSAHS.

Definitive diagnosis of OSA is made by sleep specialists with a formal sleep study or a *PSG*. A PSG is an involved study, performed at sleep study centers, that examines nocturnal sleeping patterns by monitoring physiologic parameters. In its most comprehensive form, the following parameters are studied: two to six electroencephalographic (EEG) channels to measure electrical activity of the brain and to document sleep cycles; two electrooculogram (EOG) channels to distinguish rapid eye movement (REM) from non-REM sleep; chin electromyogram (EMG) to monitor arousal and activity of the upper airway (genioglossus and digastric muscles); an airway microphone to monitor airflow from the nose and mouth; elastic belts placed on the chest and abdomen to monitor respiratory effort; an infrared video camera to monitor body position; one channel of electrocardiogram (ECG) to monitor cardiac activity; a pulse oximeter to monitor oxygen saturation; and two-leg EMG channels to monitor leg movements. A PSG may be ordered to definitively diagnose a sleep disorder, as part of medical management, or in the surgical workup of a high-risk population (e.g., preoperative screening of bariatric surgical candidates).

A PSG will diagnose the presence of OSAHS, type (central, peripheral, or mixed), and grade severity. Results are reported in as the total number of apneas and hypopneas per hour of sleep or the *AHI*. Values of 6 to 20, 21 to 40, and greater than 40 represent mild, moderate, and severe OSA, respectively.

- Mild OSA = AHI of 6 to 20
- Moderate OSA = AHI of 21 to 40
- Severe OSA = AHI of > 40

The total number of arousals hourly is the *Arousal Index* (AI).

- AI = arousals/hour.

The sum of the AHI and the AI is the Respiratory Disturbance Index (RDI).

- RDI = AHI + AI

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A.5. What are the different types of OSA?

Sleep-disordered breathing in children and adults is distinct in pathophysiology, clinical presentation, and therapy.

Childhood obstructive sleep apnea (COSA) consists of a continuum from snoring, to upper airway resistance syndrome, to the fully expressed syndrome. The pathophysiology of COSA is most commonly peripheral in origin, due to nocturnal airway blockage from nasal pathophysiology, hypertrophic tonsils and adenoids, or craniofacial dysostoses. The symptomatology in COSA consists of snoring (usually continuous), rare daytime sleepiness, and frequent behavioral disturbances (e.g., attention deficit hyperactivity disorder [ADHD]). It is distinguished from adult OSA by the following: snoring is more continuous, there is no sex predilection, and surgery (commonly adenotonsillectomy, rarely uvulopalatopharyngoplasty) is curative. There is no gold standard for the PSG diagnosis in children.

Adult OSA or OSAHS consists of a continuum from asymptomatic, to paraoxysmal snoring, to severe nocturnal airway closure, requiring the patient to sleep in a sitting position, and daytime somnolence. The pathophysiology of OSAHS is central, peripheral, or mixed. Peripheral disease is caused by redundant adipose tissue in the upper airway, in the setting of severe obesity, sometimes with a superimposed craniofacial dysostosis. The symptomatology of OSAHS consists of intermittent snoring, apneic episodes, with daytime somnolence. OSH syndrome, a milder form of OSA, may be clinically indistinguishable. *Obesity–hypoventilation syndrome* (*OHS*) is severe OSA with chronic daytime hypoventilation, SO, and hypercapnia not related to pulmonary disease. *PS* is OHS with cor pulmonale.

Patients presenting to the operating room commonly have not received a sleep study, or even a clinical diagnosis, so it is incumbant on the anesthesiologist to ask provocative questions (e.g., solicit a history of snoring, daytime somnolence, and obligate mouth breathing), and perform a targeted physical examination (e.g., check for poor Mallampati score, increased neck circumference, relative or absolute micrognathia, increased abdominal girth). So that appropriate modifications in the perioperative plan may be instituted, as will be outlined in the next sections.

American Academy of Pediatrics. Section on pediatric pulmonology, subcommittee on obstructive sleep apnea syndrome. American Academy of Pediatrics: clinical practice guidelines: diagnosis and management of childhood obstructive sleep apnea syndrome. *Pediatrics*. 2002;109:704.

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A.6. What is the Pickwickian syndrome (PS)? What is the pathogenesis of severe OSA?

The PS was so named by Burwell in 1956, as a reference to Joe, an obese, somnolent boy in the *Posthumous Papers of the Pickwick Club*, written in 1837 by Charles Dickens. With Joe, Dickins had provided the first accurate description of the most severe type of OSA, consisting of a BMI more than 50 kg per m^2 or SO, alveolar hypoventilation (hypoxemia and hypercarbia), heavy nighttime snoring with periodic respiration, hypersomnolence (daytime somnolence), secondary polycythmia, right and left ventricular hypertrophy, and right heart failure. This syndrome may occur with or without pulmonary hypertension.

The complete PS, rarely seen, consists of massive obesity, daytime somnolence, alveolar hypoventilation, periodic nighttime respiration, secondary polycythemia, right ventricular hypertrophy, and failure. In these individuals, there are repeated cycles of sleep, arousal, sleep, accompanied by obstructed breathing, with snoring and restlessness. Hypoxemia and hypercarbia result from disruption of a normal sleep pattern; with loss of REM sleep and cardiovascular changes. Loss of REM sleep induces hypersomnolence, personality, behavior, and cognitive changes, and predisposes these individuals to be accident prone. Eventually severe OSA leads to OHS, with nocturnal, and later diurnal alterations in the control of breathing, manifested as central apneic events, or apnea without ventilatory efforts. They also develop an alveolar–arterial oxygen gradient by ventilation–perfusion mismatch. The major factor in the pathogenesis of this syndrome is unknown, but may be due to decreased hypoxic and hypercarbic ventilatory drive. Later in the disease process, there is progressive daytime hypoxia and hypercarbia. When cor pulmonale supervenes, the PS is complete.

There are several cardiovascular changes in severe OSA, all related to the episodic airway closure, with hypoxemia and hypercarbia. Hypoxemia and alterations in autonomic tone may induce bradycardia during apneic episodes; in half of these patients long sinus pauses, second-degree heart block, and ventricular ectopy may result. These arrhythmias may lead to nocturnal angina and myocardial infarction in susceptible individuals. Pulmonary hypertension may be caused directly by hypoxic pulmonary vasoconstriction, or indirectly by either increased transmural pulmonary artery pressures from negative thoracic pressure created by a sustained ventilatory effort against the upper airway obstruction, or by increases in pulmonary artery tone from increased sympathetic tone created by episodic hypoxemia. Pulmonary hypertension initially causes right ventricular hypertrophy, resulting in a higher right ventricular end-diastolic pressure (RVEDP), and later culminates in right ventricular failure, or cor pulmonale. The systemic circulation is also affected by episodic increases in sympathetic tone, with systemic hypertension presenting early, and left ventricular hypertrophy, followed by left ventricular

failure presenting much later. Systemic hypertension may also lead to increased stroke rate.

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Burwell CB, Robin ED, Whaley RD, et al. Extreme obesity associated with alveolar hypoventilation: a pickwickian syndrome. *Am J Med*. 1956;21:811–818.

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Teichtahl H. The obesity-hypoventilation syndrome revisited. *Chest*. 2001;120:336–339.

A.7. What is the association between obesity and OSA? What is the etiology of pharyngeal pathology in severe obesity? Are all of the changes in the airway confined to the upper airway in obese patients with OSA?

Obesity and OSAHS are both common and coexisting diseases. Obesity has reached epidemic proportions in the industrialized world, and currently poses a greater worldwide health risk than does malnourishment. In the United States alone, obesity is annually responsible for 300,000 premature deaths and an annual healthcare cost of $100 billion. Sixty-five percent of the US population, or 127 million adults, are obese. The prevalence of severe obesity, a strong risk factor for OSAHS, is 3.15% in men and 6.70% in women (according to US population data).

Sixty percent to 90% of patients with OSAHS are obese, and it has been estimated that 9% of women and 24% of men in the United States suffer from the syndrome, a total of 18 million individuals, of which 2% of women and 4% of men are symptomatic. These figures will almost certainly increase, as the demographics shift toward an older and more obese population. Many of these patients are undiagnosed at the time of surgery, representing potential perioperative complications.

There are two reasons why severe obesity per se may cause or exacerbate OSAHS. First, there is an inverse relation between obesity and pharyngeal volume. The pharyngeal area decreases in obesity from deposition of adipose tissue into pharyngeal structures: (colon) in particular, the uvula, the tonsils, the tonsillar pillars, the tongue, the aryepiglottic folds, and, most importantly, the lateral pharyngeal walls. The volume of adipose in the lateral pharyngeal walls correlates with the clinical severity of airway obstruction. Increased deposition of pharyngeal adipose increases the likelihood that relaxation of the upper airway muscles will result in collapse of the soft-walled retroglossal space, or the oropharynx, between the uvula and the epiglottis. The shape of the pharynx remodels from an ellipse with the long axis transverse, to an ellipse with the long axis anterior–posterior. The muscles that open the collapsible pharynx on expiration during sleep (e.g., tensor palatini, genioglossus, and hyoid muscles) in response to stretch receptors in the pharynx are located in the anterior pharynx, and do not function well with a remodeled pharynx.

Second, the patency of the collapsible pharynx is determined by the transmural pressure (the difference between the extraluminal and intraluminal pressure) and the compliance of the wall. If the compliance of the wall and intraluminal pressure (inspiratory pressure) are constant, then the remaining important determinant of upper airway patency is extraluminal pressure. In obese patients, extraluminal pressure is increased by superficially located fat masses; that is, the upper airway is compressed externally. Therefore, neck circumference is greater in obese patients with OSAHS compared with obese non-OSAHS patients. The incidence and severity of OSAHS correlates better with neck circumference than does BMI. Neural control of the more than twenty pairs of muscles (especially the pharyngeal dilator muscles)

is under the control of mechanoceptors and neural signals to the hypoglossal motor neurons through the superior laryngeal or glossopharyngeal nerves to the nucleus of the solitary tract.

There are also lower airway changes in obese individuals with OSAHS. Obesity, particularly central obesity, increases visceral fat volume, resulting in decreased lung volume. According to the lung volume hypothesis, lung volume reduction decreases longitudinal tracheal wall traction, causing increased pharyngeal wall collapsibility. The trachea moves caudally during spontaneous inspiratory breathing and causes longitudinal traction on the pharyngeal wall, subsequently unfolding the mucosa and stiffening the airway.

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Isono S. Obstructive sleep apnea of obese adults: pathophysiology and perioperative airway management. *Anesthesiology*. 2009;110(4):908–921.

www.surgeongeneral.gov/topics/obesity. Official site of the surgeon general. Source of demographic trends. 2011.

A.8. What are the anesthetic implications of OSA?

Management of anesthesia in patients with severe OSAHS poses significant risks. These patients are extremely sensitive to minimal doses of central nervous system depressant drugs, such as anesthetics, sedatives, and analgesics, and may exhibit prolonged sedation, resedation, or apnea, as well as upper airway obstruction or, rarely, massive pharyngeal collapse. For these reasons, premedication with benzodiazepines or narcotics is used sparingly if at all, and sedation is generally reserved for painful or unpleasant situations (e.g., placement of invasive lines) where the patient is under the direct observation of a trained clinician.

Difficult tracheal intubation is expected in 13% to 24% of obese patients with OSAHS. In this particular case, the patient presents for laparoscopic bariatric surgery. Although the "ideal general anesthetic" regimen for these patients is a matter of some discussion, the literature does support the following: a safe induction, a deep maintenance anesthetic with muscle relaxants, and a smooth emergence with rapid offset devoid of active metabolites or trace anesthetic. Anesthetic gases should be insoluble, resistant to metabolic degradation, and without lipid depot compartmentalization, combined with rapid return of airway reflexes. The only weak inhalation anesthetic, nitrous oxide (N_2O), has the advantage of being relatively insoluble, as measured by blood–gas solubility coefficient (0.46), but it causes intestinal inflation, may be emetic, and is not recommended in the presence of pulmonary hypertension, a condition that is more common in MO. Of the available potent inhalation anesthetics (desflurane, sevoflurane, and isoflurane), desflurane combines the quickest wake-up, fastest return of airway reflexes, lowest solubility, as measured by the blood–gas solubility coefficient (desflurane, 0.45; sevoflurane, 0.65; and isoflurane, 1.4), and lowest percentage of hepatometabolization (desflurane, 0.02%; isoflurane, 0.2%; sevoflurane, 4% to 5%). Intravenous agents should be either lipophobic (hydrophilic), spontaneously degrade in vivo, or be ultrashort acting.

Sedation or awake fiberoptic intubation: ketamine and dexmedetomidine are optimal agents. *Induction of general anesthesia:* all agents have been utilized. *Maintenance agents:* air/oxygen mixtures, desflurane, cisatracurium, and remifentanil. *Last hour of general anesthesia and emergence:* nitrous oxide (except in the presence of pulmonary hypertension), remifentanil, and morphine sulfate.

When feasible, regional anesthesia is useful. Tracheal extubation is considered only when patients are fully awake with intact upper airway reflexes. Episodic arterial hypoxemia may occur early, in the first 24 hours, or late, from the second to the fifth day, postoperatively.

Discharge from the postanesthetic care unit (PACU) may be made in the morbidly obese OSA, per protocol, after they have been started on CPAP or bilevel positive airway pressure (BIPAP), and have been observed for at least 30 minutes, without stimulation, and found to be free of respiratory arrests. If they have even one respiratory arrest, PACU stay is extended for an additional 3 hours, and consideration is made to transfer the patient to a monitored bed.

Intravenous patient-controlled analgesia (PCA) appears to be well tolerated in the morbidly obese, without deleterious effects on oxygen saturation, respiratory function, blood pressure, or heart rate. Dosing is based on IBW, without continuous rate. Although the gold standard in acute pain management is still morphine sulfate (starting at 20 μg per kg every 10 minutes with a 4 hour dose of 80% of the calculated.maximum dose), hydromorphone has largely supplanted morphine, due to its "one size fits virtually all" profile (starting at 0.2 mg every 10 minutes, progressing to 0.3 mg every 10 minutes, down to 0.1 mg every 15 minutes if excessive). Hydromorphone has less histamine release and nausea and vomit than morphine sulfate. Morphine sulfate and rarely fentanyl are emerging as second line IV PCA agents. Of course, it is important to individualize therapy. It is never appropriate to add a continuous rate in this patient population.There is a paucity of literature on the safety and efficacy of intravenous PCA in the morbidly obese severe OSAHS patient. There are case reports of respiratory complications in this population; postoperative pain management must take into account the exquisite sensitivity of these patients to the ventilatory-depressant effects of opioids.

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A.9. What kind of metabolic problems would you expect to find in morbidly obese patients?

In MO, there is an increase in both low metabolically active tissue (e.g., adipose) and normally active tissue (e.g., muscle). In general, lean body weight (LBW) is equal to IBW plus 20% to 40% IBW. IBW is a value, based on population demographics, which could never be realized through weight reduction in a severely obese individual.

Morbidly obese individuals have an increase in total oxygen consumption and carbon dioxide production due to an increased tissue mass. Increased metabolism demonstrates a linear relation with body weight and body surface area. Basal metabolic rate, however, remains normal in obese individuals.

Leptin is a hormone that is derived from adipose tissue, and is involved in lipid metabolism. Leptin serves a key role in metabolism, It signals the appetite center in the hypothalamus to promote satiety when the individual has eaten an adequate portion. Obese patients have a higher serum leptin level, possibly as a result of leptin resistance, and consequently have an abberant satiety response. OSA patients have an even higher serum leptin level than BMI-matched non-OSA patients. Short-term CPAP therapy decreases serum leptin levels. Leptin appears to have a role in respiratory control in obese patients. It prevents respiratory depression. Excessive visceral adipose tissue has been implicated in metabolic syndrome, via the secretion of hormones and proinflammatory cytokines.

Alam I, Lewis K, Stephens JW, et al. Obesity, metabolic syndrome and sleep apoea: all pro-inflammatory states. *Obes Rev.* 2007;8:119–127.

Chin K, Shimizu K, Nakamura T, et al. Changes in intra-abdominal visceral fat and serum leptin leves in patients with obstructive sleep apnea syndrome following nasal continuous positive airway pressure therapy. *Circulation.* 1999;100: 706–712.

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Hines RL, Marschall KE. *Stoelting's Anesthesia and Co-existing Disease.* 5th ed. Philadelphia: Churchill Livingstone, Elsevier; 2008:297–306.

A.10. Describe the changes that occur in the following respiratory parameters in morbidly obese patients:

- *Pulmonary mechanics* : tidal volume (V_T), functional residual capacity (FRC), residual volume (RV), vital capacity (VC), inspiratory reserve volume (IRV), expiratory reserve volume (IRV), and total lung capacity (TLC)
- Flow volume loops
- Pressure volume loops
- Diffusing capacity for carbon monoxide (DLCO)
- *Compliances*: lung, chest wall, and total
- *Resistance*: airway and total respiratory system
- Closing capacity
- Work of breathing

Morbidly obese patients have reduced lung volumes, increased work of breathing, and alterations in control of breathing and gas exchange. Body fat distribution, as well as BMI, determines the effect of obesity on pulmonary function.

Pulmonary mechanics. Pulmonary function tests (PFTs), or lung volumes, are uniformly altered in obesity. V_T is normal or increased in the obese, and is decreased in Pickwickian obesity. IRV is decreased. ERV is markedly decreased, because the increased weight of the torso decreases the normal expansive tendency of the rib cage and pulmonary parenchyma. RV is normal. FRC or ERV plus RV, is markedly decreased, because of the decrease in ERV. VC or ERV + V_T + IRV, is decreased because of decreased ERV. TLC or RV + ERV + V_T + IRV, is decreased for the same reason as VC. Individuals with central, as opposed to peripheral fat distribution, have greater decreases in the FVC, forced expiratory volume (FEV), and TLC. The maximum voluntary ventilation (MVV) may also be reduced.

Diffusing capacity for carbon monoxide. The DLCO is usually normal in individuals with obesity and mildly reduced in those with OHS, because the lung parenchyma is normal, and changes in PFTs are due to abnormal chest wall mechanics and lower lung volumes. DLCO is a useful test to separate intrinsic lung pathology from obesity.

Compliance. There is a decrease in the total respiratory system compliance ($1/C_T = 1/C_L + 1/C_{CW}$), where C_T is the total compliance, C_L is the compliance of the lung, and C_{CW} is the compliance of the chest wall. Total compliance is always decreased because of the weight of the torso and abdominal contents pressing against the diaphragm creating a restrictive component, markedly decreasing the chest wall compliance. Lung compliance is often normal, but is decreased when pulmonary and circulatory comorbidities are present (e.g., pulmonary hypertension).

Resistance. There are increases both in the airway resistance (reduced elastic tension of the lung) and in the total respiratory system resistance (increased elastic tension of chest wall) at lower lung volumes, which leads to reduction in the caliber of the smaller airways. The increase in total resistance is approximately 30% in simple obesity, and 100% in OHS. Resistance increases further in the supine position, possibly due to extrinsic adipose pressure of the supralaryngeal airway, and a decreased FRC.

Closing capacity. FRC is reduced in the morbidly obese patient, and may be below the closing capacity, resulting in small airway closure, ventilation–perfusion mismatch, right-to-left shunting, and possibly hypoxemia, the so-called positional ventilatory collapse. This may be worsened in the supine position, Trendelenberg position, by general anesthesia and muscle relaxants, and improved by the use of lung recruitment strategies (e.g., PEEP), and reverse Trendelenberg position.

Increased work of breathing. MO is associated with a 70% increase in the work of breathing, and a fourfold increase in the oxygen cost of breathing (oxygen consumed by the respiratory muscles per liter of ventilation, used as a surrogate for the energy cost of breathing). This is due to decreased lung compliance, increased respiratory resistance, and threshold inspiratory load from adipose tissue mass. Obese individuals with obstructive sleep apnea syndrome (MO-OSAHS) have elevated pharyngeal and nasopharyngeal resistance, raising the work of breathing 60% above the obese, and 250% above the nonobese.

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Jones RL, Nzekwu MM. The effects of body mass index on lung volumes. *Chest*. 2006;130:827–833.

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Parameswaran K, Todd DC, Soth M. Altered respiratory physiology in obesity. *Can Respir J*. 2006;13:203–210.

Zavorsky GS, Hoffman SL. Complications of obesity. Pulmonary gas exchange in the morbidly obese. *Obes Rev*. 2008;9:326–339.

A.11. What changes occur in Pao_2 and $Paco_2$ in morbidly obese patients?

Hypoxemia is the most common blood gas abnormality in the severely obese patient. The etiology is most commonly due to a low ventilation/perfusion ratio, and less commonly as a result of hypoventilation. Pulmonary perfusion is increased in the obese as a result of increased CO, increased circulating blood volume, and, occasionally, pulmonary hypertension. Alveolar ventilation is decreased in the obese as a

result of upper airway closure, and spirometric changes (decreased ERV, and FRC). In addition, the closing volume is often greater than the expiratory reserve volume, particularly in the supine position, causing airway closure, resulting in right-to-left shunt and hypoxemia.

The second most common blood gas abnormality in the severely obese is a variable change in the carbon dioxide tension ($Paco_2$), not related to lung disease, and dependent on the alveolar ventilation. There are three patterns of ventilatory derangement described in the following:

- *Alveolar hyperventilation* in response to a hypoxic drive. This occurs in young, active subjects. $Paco_2$ is approximately 35 mm Hg.
- *Periodic, nocturnal, alveolar hypoventilation* with normal daytime values. This is the hallmark of OSAHS.
- *Daytime, or constant, alveolar hypoventilation*. This occurs in OHS, and PS.

Hines RL, Marschall KE. *Stoelting's Anesthesia and Co-existing Disease*. 5th ed. Philadelphia: Churchill Livingstone, Elsevier; 2008:297–306.

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A.12. What changes occur in intrapulmonary shunt (Q_S/Q_T) and dead space (V_D/V_T) in morbidly obese patients? Describe the equations.

Q_S/Q_T is normally less than 5%. In the morbidly obese, this is increased, because of the following:

- Lower ventilation/perfusion ($\dot{V}/\dot{Q}$) ratio
- Upper airway closure (e.g., OSAHS)
- Decreased FRC, from abdominal compression
- Hypoventilation (e.g., OSAHS)
- Increased pulmonary circulation, from increased CO, increased blood volume, and occasionally pulmonary hypertension

$$\text{Shunt equation} = Q_S/Q_T = (Cc_{O_2} - Cao_2)/(Cc_{O_2} - Cv_{O_2})$$

where Cc_{O_2} is pulmonary capillary oxygen content; Cao_2 is arterial oxygen content; Cv_{O_2} is mixed venous oxygen content.

Dead space is anatomic, alveolar, or physiologic. *Anatomic dead space* is the volume of the lung and upper airway that is not involved in gas exchange. Ventilation of this area does not result in gas exchange. The volume of the anatomic dead space in milliliters is approximately equal to the IBW in pounds. Fowler's method of measuring anatomic dead space is by analyzing nitrogen concentration after single breath 100% oxygen. *Alveolar dead space* is the area of alveoli with ventilation and no perfusion, which has a $\dot{V}/\dot{Q}$ equal to infinity, or West Zone 1. *Physiologic dead space*, the sum of anatomic and alveolar dead space, is the total area of lung plus airways not involved in gas exchange. Physiologic dead space is approximately 30% of the V_T. It is decreased in the supine position, and increased with disease states that alter $\dot{V}/\dot{Q}$, and in OHS, because the latter individuals adopt a shallow ventilatory pattern. Physiologic dead space is decreased in the obese, due to increased V_T ventilation and unchanged anatomic dead space. Physiologic dead space, or V_D/V_T, is measured by the Bohr equation.

$$\text{Bohr equation: } V_D/V_T = (Paco_2 - P_{E}co_2)/Paco_2$$

where $P_{E}co_2$ is mixed expired CO_2 tension.

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A.13. What is the impact of pneumoperitoneum (PNP) on the respiratory and cardiovascular system of the bariatric surgical patient? Are there any other effects?

Currently, many surgical procedures, including bariatric surgery, are performed by laparoscopy. The peritoneal cavity is inflated through a trocar with carbon dioxide at a pressure of approximately +15 cm H_2O to displace the abdominal wall, and improve working and visualization conditions for the surgeons. Oxygenation, lung, and chest wall compliance decrease, and peak inspiratory and mean airway pressures increase as a result. These values are further decreased by Trendelenburg position, but may not be improved by reverse Trendelenburg, although this is controversial. Respiratory mechanics are worsened by PNP, due to decreased compliance and increased airway resistance. Increased V_T ventilation or ventilatory rate does not improve oxygenation, as long as closing capacity has been exceeded by FRC. Large V_T ventilation has been associated with volutrauma and low lung water pulmonary edema. Although otherwise healthy morbidly obese patients tolerate these changes relatively well, some patients may require lung recruitment strategies, such as the use of pressure mode ventilation, inspiration/expiration ratio of 1:1, and PEEP. Settings should be carefully adjusted to maintain normocarbia, as judged by end-tidal carbon dioxide, and readjusted as conditions change.

PNP effects on the cardiovascular system occur through increases in the systemic vascular resistance and the mean arterial pressure (MAP). There is a biphasic pattern: When inflation pressure is below 10 mm Hg, increased venous return, by splanchnic sequestration, raises MAP and CO. When inflation pressure is above 20 mm Hg, the inferior vena cava is compressed, resulting in decreased venous return, decreasing MAP and CO. PNP and reverse Trendelenburg position may decrease femoral venous blood flow, resulting in venous stasis in a patient population already predisposed to venous thromboembolism.

Increased sympathetic output from from PNP may result in decreased urine output by a 30% to 50% decreased glomerular filtration rate; postoperative renal function is normal. PNP and Trendelenburg position cause cephalad migration of the tracheal tube, and may precipitate endobronchial intubation.

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A.14. What changes occur in the cardiovascular system of the obese patient? Discuss cardiac output (CO), blood volume, blood pressure, and pulmonary arterial pressure.

MO produces changes in cardiac morphology and ventricular function.

As BMI increases, both total and circulating blood volume increase. Although absolute blood volume is expanded, relative blood volume is decreased. Increase in circulating blood volume and decrease in systemic vascular resistance results in augmentation in CO. CO increases by increased stroke volume, and heart rate remains unchanged. CO and stroke volume increase in proportion to oxygen consumption and the degree of obesity, but more closely to the LBW. Left ventricular (LV) wall stress increases according to the law of Laplace ($P_2 - P_1 = 2T/R$), where P is the change in pressure produced by the increased volume, T is the LV wall stress, and R is the radius. Increase in afterload from hypertension produces eccentric LV hypertrophy, and eventually LV dysfunction. They are therefore sensitive to acute changes in preload and afterload. Morbidly obese patients presenting to the operating room require an ECG, chest radiographs, and an echocardiogram. Seventy percent of the echocardiograms in morbidly obese patients contain abnormalities.

Hypertension is more prevalent because of increased CO and increased blood volume. Hypertension is more commonly systolic than diastolic in the obese. Obese patients without comorbidity have normal pulmonary artery filling pressures. Those individuals with OHS and PS, however, commonly have pulmonary hypertension, as a result of hypoxic pulmonary vasoconstriction and increased CO. Hypertension and increased CO lead to congestive heart failure in approximately 10% of obese individuals. There are two mechanisms in the pathogenesis of heart failure. In the first, pulmonary and systemic vascular congestion develops as a consequence of chronic volume overload superimposed on diminished diastolic compliance, caused by long-standing ventricular hypertrophy. In the second, chronic volume overload and high CO results in LV hypertrophy. The ventricular wall/cavity ratio decreases, and LV systolic dysfunction results. Echocardiography demonstrates LV hypertrophy in these patients, often in the absence of electrocardiographic evidence. Obesity leads to fatty infiltration of the cardiac conduction system, predisposing to sudden death. Obesity is not a direct predictor of coronary artery disease. As an indirect predictor, obesity is linked to coronary artery disease through hyperlipidemia and systolic hypertension.

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Tsang TS, Barnes ME, Miyasaka Y, et al. Obesity is a risk factor for the progression of paraoxysmal to permanent atrial fibrillation: a longitudinal cohort study of 21 years. *Eur Heart J*. 2008;29:2227–2233.

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A.15. Are there any other disease entities commonly associated with obesity?

Secondary obesity may be associated with hypothyroidism, Cushing disease, insulinoma, hypogonadism, and hypothalamic disorders. Although most obese patients are not diabetic, 80% to 90% of nonketotic diabetics are obese. Increased insulin secretion and insulin resistance resulting from peripheral tissue insensitivity are well-characterized features of obesity. Obesity exacerbates the diabetic state. Furthermore, malignancies of breast, prostate, cervix, uterus, colon, and rectum are more common in the obese.

In addition, there is a disproportionate increase in health-related risks from obesity. Above a BMI of 25, the risk of coronary artery disease more than doubles. Above a BMI of 29, there is an increased perioperative risk of pulmonary embolus. Above a BMI of 35, there is more than a 40-fold increase in adult-onset diabetes mellitus, respiratory disease, osteoarthritis, and OSAHS. Perioperative mortality during weight reduction surgery is statistically correlated with BMI, preoperative hypertension, anastomotic leak, and pulmonary embolus. A combination of central obesity, hypertension, dyslipidemia, and impaired glucose tolerance is termed *metabolic syndrome* and increases risk for morbidity and death.

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Ioannidis I. The road from obesity to type 2 diabetes. *Angiology*. 2008;59(2 suppl):39S–43S.

Kushner R. Evaluation and management of obesity. In: Fauci AS, Braunwald E, Kasper DL, et al., eds. *Harrison's Principles of Internal Medicine*. 17th ed. New York: McGraw Hill; 2008;75:468–473.

Peterson LR. Obesity and insulin resistance: effects on cardiac structure, function, and substrate metabolism. *Curr Hypertens Rep*. 2006;8:451–456.

A.16. What anatomic changes that affect the airway are associated with MO?

Patient-specific anatomic changes in the MO are related to the BMI, type of obesity (peripheral vs. central), and presence or absence of OSAHS. Not all morbidly obese patients have airway involvement. The anatomic changes affecting the airway are not always easily diagnosed on routine physical examination. At a given BMI, there is more airway involvement in central obesity compared with peripheral obesity, and the most severe involvement airway involvement occurs in patients with OSAHS.

Significant anatomic alterations in the airway of the morbidly obese include the following:

- Deposit of adipose tissue in the lateral pharyngeal walls, and to a lesser extent in the uvula, the tonsillar pillars, the tongue, and the aryepiglottic folds, causing a

decreased in the pharyngeal area. Adipose deposition in the false vocal folds may render the glottic opening difficult to recognize, even with the vocal cords abducted.
- Deposit of adipose tissue external to the upper airway (lateral parapharyngeal fat pads, or jowls), extrinsically compressing the airway.
- Presence of hypopharyngeal adipose tissue not evident on external examination that acts as a ball valve, obstructing the upper airway and interfering with the line-of-sight at direct laryngoscopy.
- Presense of pretracheal adipose tissue, which pushes the hyoid bone posteriorly into a less favorable position, causing the epiglottis to partially override the glottic entrance, worsening the laryngoscopic view.
- Alteration in shape of the pharynx from an ellipse with the long axis lateral transverse to an ellipse with the long axis anterior–posterior.
- Decreased efficiency of the anterior pharyngeal dilator muscles (tensor palatini [nasopharynx], genioglossus [oropharynx], hyoid muscles [laryngopharynx]), which promotes snoring.

The anatomic changes that occur with MO are important for three reasons. First, these patients may obstruct their airway with light to moderate sedation (peripheral OSAHS). Various surgical procedures have been developed to improve this problem, such as the uvulopalatopharyngoplasty. Second, these patients may be difficult to mask ventilate, both because of external adipose tissue, and internal collapse of redundant upper airway adipose. Third, there is a higher incidence of difficult intubation (DI) and failed intubation in MO. When coupled with the precipitous desaturation, there is a need to revise the ASA's Difficult Airway Algorithm.

The literature is inconclusive on the relation between obesity and DI. According to some authorities, obesity is an independent risk factor for DI, due to a disproportionately large tongue base, or a short, thick neck. Other authors found that a higher BMI is not an indicator of DI, but that increased neck circumference and poor Mallampati scores (classes 3 and 4) are. MO-OSAHS patients with other risk factors for DI (e.g., micrognathia) develop worsening of airway closure to an even greater degree than their counterparts.

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Kheterpal S, Han R, Tremper KK, et al. Incidence and predictors of difficult and impossible mask ventilation. *Anesthesiology*. 2006;105:885–891.

Peterson GN, Domino KB, Caplan RA, et al. Management of the difficult airway: a closed claims analysis. *Anesthesiology*. 2005;103:33–39.

Practice guidelines for management of the difficult airway: an apdated report by the American Society of Anesthesiologists Task Force on Management of the Difficult Airway. *Anesthesiology*. 2003;98:1269–1277.

A.17. What derangements of the gastrointestinal system are associated with MO?

There are several changes in the upper gastrointestinal tract that place severely obese individuals at risk for acid aspiration pneumonitis upon induction and emergence

of general anesthesia: prolonged gastric emptying time, decreased gastric pH, increased incidence of hiatal hernia, linear increase in intra-abdominal pressure with increasing body weight, and impaired gastroesophageal antireflux mechanism. Ninety percent of fasting morbidly obese patients exceed Mendelson's criteria, a gastric volume of greater than 0.35 mL per kg total body weight (TBW), with a pH less than 2.5.

There is a substantially higher incidence of hepatobiliary disease in the morbidly obese, such as cholelithiasis, hepatitis, intrahepatic and extrahepatic cholestasis, hepatic steatosis, and cirrhosis. Seventy-five percent of the morbidly obese have hepatic steatosis. Although there is a 25% incidence of severe hepatic dysfunction in the morbidly obese, there is no clear correlation between LFTs and hepatic dysfunction, complicating medical and anesthetic management. Pancreatic disease is also more common in this population, specifically gallstone pancreatitis, adult-onset diabetes mellitus, and insulinoma. There is a higher incidence of colorectal malignancies in the morbidly obese.

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B. Preoperative Evaluation and Preparation

B.1. How would you evaluate this patient preoperatively?

Preoperative evaluation should include a detailed history, review of systems, physical examination, and laboratory tests. Special attention should be paid to circulatory, pulmonary, and hepatic functions. Circulatory evaluation includes signs and symptoms of left or right ventricular failure, history of hypertension, and electrocardiographic abnormalities. Respiratory evaluation includes smoking history, exercise tolerance, history of hypoventilation and somnolence, pulmonary function tests with spirometry and baseline arterial blood gases, and chest x-ray results. Hepatic function tests include serum albumin and globulin, serum aspartate aminotransferase, serum alanine aminotransferase, direct and total bilirubin, alkaline phosphatase, prothrombin time, and cholesterol levels.

A cardiology consultation is needed, with a noninvasive assessment of function by echocardiogram. Patients without an adequate echocardiographic window require radionucleotide ventriculography to assess ventricular function and morphology. It is important to obtain a full assessment by the cardiologist, to determine whether this patient is optimized, and which invasive lines, if any, are appropriate. This patient was found to have mild right ventricular hypertrophy and mild pulmonary artery hypertension. Pertinent negatives were the absence of demon-

strated coronary artery disease, and left or right ventricular failure. In this case, it was determined that the patient was optimized, and that an arterial line would be helpful.

Physical examination focuses on the cardiovascular, pulmonary, and the upper airway. The upper airway assessment, in particular, should be thorough. In addition to the routine parameters, atlanto-occipital joint extension, Mallampati classification, temporomandibular joint assessment with interincisor distance, mentohyoid distance, and dentition, the following parameters should be checked: pretracheal adipose thickness, neck circumference, and hypertrophic tonsils and adenoids. Nonreassuring findings related to the latter three variables are a large neck, an abundance of anterior neck soft tissue, and obligate mouth breathing. Neck circumference is an independent predictor of DI; the odds ratio is 1:13. At 40 cm (15.75 in.), there is a 5% chance of DI; at 60 cm (23.62 in.), this increases to 35%. Pretracheal adipose greater than 1 in. (2.5 cm) at the level of the vocal cords, determined by ultrasonography, may be an even better independent predictor of DI. Obligate mouth breathing may be a clue that the patient has adenotonsillar hypertrophy, nasal septal blockage, or a craniofacial dysostosis.

Factors that render difficult mask ventilation (DMV) should be noted. According to Langeron, DMV risk factors are age over 55 years, BMI greater than 26 kg per m^2, history of snoring, presence of a beard, and incomplete dentition. According to Kheterpal, DMV and DI risk factors are limited mandibular protrusion, increased neck circumference, OSA, history of snoring, and BMI over 30 kg per m^2. Redundant adipose tissue may hide physical findings suggestive of a DI (e.g., increased submandibular angle).

Prior anesthetic records should be obtained. Patients with a history of heavy snoring should have a formal sleep study or PSG. Severity of OSAHS, AHI, home oxygen therapy with CPAP or BIPAP, response and compliance should be noted.

The incidence of claims for severe morbidity and death has significantly decreased since release of the practice guideline for management of the difficult airway by the ASA.

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Suzuki N, Isono S, Isikawa T, et al. Submandibular angle in nonobese patients with difficult tracheal intubation. *Anesthesiology*. 2007;106:916–923.

Tsai WH, Remmers JE, Glidden DV, et al. A decision rule for diagnostic testing in obstructive sleep apnea. *Am J Respir Crit Care Med*. 2003;167:1427–1432.

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B.2. Interpret the following arterial blood gas: pH 7.25; $Paco_2$ 50 mm Hg; Pao_2 58 mm Hg; and HCO_3^- 25 mEq/L on room air.

This blood gas indicates respiratory acidosis and metabolic acidosis with hypoxemia. HCO_3^- 25 mEq per L is a laboratory error. A pH level of 7.25 is acidosis, which may be respiratory, metabolic, or both. If no metabolic abnormality is present, a Pco_2 of 50 mm Hg should produce a pH level of 7.35 (Table 62.1). The difference in pH (7.35 − 7.25 = 0.10) is due to metabolic acidosis. For each 7 mEq per L of acid or base increase, pH changes 0.10 unit in the appropriate direction. A metabolic acidosis of 0.1 unit pH is equivalent to a 7-mEq per L base deficit. The HCO_3^- is expected to be 17 mEq per L (24 − 7 = 17), but a change in $Paco_2$ itself will change the HCO_3^- from chemical equilibrium. Each 10-mm Hg increase in $Paco_2$ from normal increases the HCO_3^- by 1 mEq in acute CO_2 retention and by 4 mEq in chromic retention. Therefore, expect the HCO_3^- to be 17 + 1 = 18 mEq in acute CO_2 retention or 17 + 4 = 21 mEq in chronic CO_2 retention. The blood gas machine provides direct measurement of the pH, $Paco_2$, and Pao_2.

The HCO_3^- is usually derived from an equation or from a nomogram. If a discrepancy is found between the pH, $Paco_2$, and the HCO_3^-, the technical error is usually in the HCO_3^-. It is important to recheck the blood gases according to clinical conditions. A $Paco_2$ of 50 mm Hg indicates alveolar hypoventilation due to decreased minute volume or increased dead space. To interpret the Pao_2, the FIO_2 must be known. A Pao_2 less than 200 Hg may indicate ventilatory failure if the FIO_2 is 1.0. Hypoxia in obese patients is usually caused by increased venous admixture from a decreased ventilation/perfusion ratio as a result of low FRC and hypoventilation. Metabolic acidosis with hypoxemia indicates lactic acidosis from anaerobic metabolism.

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B.3. What is the equation for blood pH?

The Henderson–Hasselbalch equation is:

$$pH = pK + \log \frac{HCO_3^-}{H_2CO_3}$$

The H_2CO_3 concentration is low and cannot be directly measured. Normal blood H_2CO_3 concentration is 0.0017 mmol per L. H_2CO_3 is proportional and not equal to

Table 62.1 Predicted pH at Different $Paco_2$ Levels in the Absence of Metabolic Acid–Base Abnormality.

$Paco_2$	pH (APPROXIMATE)
80	7.20
60	7.30
40	7.40
30	7.50
20	7.60

Each 10-mm Hg decrease in $Paco_2$ from normal increases the pH 0.1 unit. Each 20-mm Hg increase in $Paco_2$ from normal decreases the pH 0.1 unit.

dissolved CO_2. Clinically dissolved CO_2 is used to replace H_2CO_3. Therefore, pK is changed to K_a. Dissolved CO_2 is calculated as αPCO_2; α being the solubility coefficient for carbon dioxide in body fluids, or 0.031 mmol/L/mm Hg PCO_2. For a normal PCO_2 of 40 mm Hg, dissolved CO_2 is calculated to be $40 \times 0.031 = 1.2$ mmol per L. The pK_a is 6.1, but this is variable with temperature and pH. The modified Henderson–Hasselbalch equation is as follows:

$$pH = pK_a + \log \frac{HCO_3^-}{dCO_2} \text{ or } pH = pK_a + \log \frac{HCO_3^-}{0.031 \times PCO_2}$$

Lumb AB. *Nunn's Applied Respiratory Physiology*, 6th ed. Philadelphia, PA: Butterworth-Heinemann; 2005:150–151.

B.4. What are the normal values for blood pK_a, dCO_2, HCO_3^-, and H_2CO_3?

The normal values are pK_a, 6.1; dCO_2,1.2 mmol/L; HCO_3^-, 24 mEq/L; and H_2CO_3, 0.0017 mmol/L.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 6th ed. Philadelphia: Elsevier Butterworth-Heinemann; 2005:149.

B.5. Interpret the following spirometry screening test: VC 2.36 L (expected 3.375 L); forced expiratory volume in 1 second (FEV_1) per forced vital capacity (FVC) 82%; and VC 70% of expected value.

Preoperative spirometric screening reveals mild restrictive lung disease, with no evidence of obstructive lung disease. *VC* is dependent on sex, age, and height. In restrictive lung disease, the VC is less than 75% of the expected value; a value of 70% is consistent with mild restrictive lung disease. The normal *ratio of FEV_1 to FVC (FEV_1/FVC)* is more than 80%; a value of 82% is normal. In obstructive lung disease, the FEV_1/FVC is less than 75%.

Here are some useful approximations: The expected VC in liters of healthy adult males is approximately equal to the height in meters squared. VC is approximately equal to 65 mL per in. or 25 mL per cm height for men, or 52 mL per in. or 20 mL per cm height for women. The *RV* is approximately equal to 30% of the VC.

Flier J, Maratos-Flier E. Biology of obesity. In: Fauci AS, Braunwald E, Kasper DL, et al., eds., *Harrison's Principles of Internal Medicine*. 17th ed. New York: McGraw Hill; 2008:462–468.

B.6. How would you premedicate this patient? Why?

No sedatives or narcotics should be given to an obese, Pickwickian patient as premedication. Light sedation may be administered to an otherwise healthy obese patient, if appropriate monitoring and qualified personnel are available to ensure vigilence. Once respiratory depressants have been administered, supplementary oxygen should be administered to prevent hypoxia from respiratory depression. Current practice is not to give sedatives or hypnotics until these patients are on the operating room table, as part of preparation for painful procedures (e.g., arterial line placement), or airway management (e.g., airway topicalization and cranial nerve blocks V, IX, and X). Even then, emphasis should be on minimal respiratory depression. We believe that a

well-conducted preoperative visit is more important than is sedation. This patient was not sedated before surgery.

When premedication is used, it should be given orally or intravenously, and not intramuscularly, as it may be inadvertently administered into adipose tissue, leading to unpredictable absorption.

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B.7. Describe weight-based dosing.

Drugs are dosed in the morbidly obese on the basis of their lipophilicity. *Highly lipophilic drugs* have increased VD for obese individuals relative to normal-weight individuals. Drug doses are calculated on the basis of the patient's TBW. Examples of this group are thiopental, propofol, benzodiazepines, fentanyl, sufentanil, dexmedetomidine, and succinylcholine. *Weakly lipophilic or lipophobic drugs* have unchanged VD. Drug doses are calculated on the basis of the patient's LBW, which is IBW plus 20% to 40% IBW. Examples of this group are alfentanil, ketamine, vecuronium, rocuronium, atracurium, cisatracurium, and morphine sulfate. *Exceptions* are lipophilic drugs with unchanged VD. Drug doses are calculated on the basis of the patient's LBW. An example of this group is remifentanil. In the calculation of weight-based dosing, it is helpful to use Internet calculators. Here is a sample calculation of appropriate dosages in our patient (in bolds are the drugs used).

Demographics: height, 5 ft 4 in. (162.6 cm); weight, 387.2 lb (176 kg); BMI, 66.6 kg per m^2. *IBW*, assuming a large frame, is 134 to 151 lb (60.9 to 68.6 kg). *LBW*, or 120% to 140% IBW is 174 to 196.6 lb (79.2 to 89.2 kg).

Note: IBW can also be derived from Broca's Index (see section A.2).

- *Highly lipophilic drugs (use TBW)*
  - **Midazolam** 2 to 6 mg background sedation for fiberoptic bronchoscopy (FOB)
  - **Dexmedetomidine** 1 μg/kg over 10 minute, followed by 0.2 to 0.7 μg/kg/hour = 176 μg over 10 minute, 35.2 to 123.2 μg/kg/hour for FOB
  - **Thiopental** 4 to 5 mg/kg × 176 kg = 704 to 880 mg bolus for induction
  - **Propofol** 1 to 2 mg/kg × 176 kg = 176 to 352 mg bolus for induction
  - **Fentanyl** 1 to 2 μg/kg = 176 to 352 μg bolus after intubation
  - **Succinylcholine** 1 to 1.5 mg/kg = 176 to 264 mg for intubation
- *Weekly lipophilic or lipophobic drugs (use LBW = 120% to 140% IBW)*
  - **Ketamine** 10 mg/dose for FOB
  - **Morphine sulfate** 10 to 20 mg in divided doses 1 hour before end of surgery
  - **Cisatracurium** 1.5 to 2 μg/kg/minute = 264 to 352 μg/minute infusion
- *Exceptions (use LBW)*
  - **Remifentanil** 0.2 μg/kg/minute = 17 μg/minute

De Baerdemaeker LE, Jacobs S, Pattyn P, et al. Influence of intraoperative opioid on postoperative pain and pulmonary function after laparoscopic gastric banding: remifentanil TCI vs sufentanil TCI in morbid obesity. *Br J Anaesth*. 2007;99:404–411.

Han PY, Duffell SB, Kirkpatrick CM, et al. Dosing in obesity: a simple solution to a big problem. *Clin Pharm Ther*. 2007;82:505–508.

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www.manuelsweb.com/IBW.htm IBW calculator for men or women.

C. Intraoperative Management

C.1. How would you monitor this patient?

In addition to the routine mandated monitors of ECG, noninvasive blood pressure, pulse oximetry, end-tidal carbon dioxide, and temperature, an arterial line is inserted for frequent assessment of blood gases and for continuous blood pressure tracing. An esophageal stethoscope with thermistor is placed in the axilla to monitor temperature, because any device placed in the esophagus may be inadvertently included in the surgical anastomosis. Hourly urine output is evaluated to assess fluid balance. A peripheral nerve stimulator is used to monitor the effects of muscle relaxants. A processed electroencephalogram, such as the bispectral index (Aspect Medical Systems, Inc., Newton, MA), was used to monitor depth of anesthesia.

The advantages of invasive monitoring have to be weighed against the possible complications. Laparoscopic bariatric surgeries have minimal blood loss (typically <100 to 200 mL) and fluid shifts. These are elective cases, and patients are optimized preoperatively. Invasive arterial monitoring is used for the super obese with severe cardiopulmonary disease or poor fit of the noninvasive blood pressure cuff because of the conical shape of the upper arms or unavailability of appropriately sized cuffs. Accurate blood pressure readings may be obtained from the wrist, as it was in this case, or the ankle. Central venous access is typically used when there are difficulties obtaining peripheral access, and was not used here. A pulmonary artery catheter is reserved for patients with documented pulmonary hypertension, cor pulmonale, or left ventricular failure.

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C.2. The ASA's Difficult Airway Algorithm provides a guideline for management of the difficult airway. How do the comorbidities of MO and OSA modify implementation of the algorithm?

The ASA's Difficult Airway Algorithm provides a guideline for management of the difficult airway. It was created by a panel of experts under the direction of the ASA in 1993 and modified in 2003. Implementation of the Algorithm will be altered in different patient populations, according to factors such as patient demographics, comorbidities, surgical requirements, equipment availability, presence of additional personnel, and probably most importantly, the skill set of the anesthesiologist.

In the severely obese patient population, with demonstrated or suspected OSA, the following considerations are relevant: patients are "full stomach" by demographics, they are vulnerable to precipitous apneic deoxygenation, the standard airway assessment may not be sufficient, there is a higher incidence of DMV and DI, and redundant adipose tissue may obstruct the line of sight on laryngoscopy.

In this patient population, the Difficult Airway Algorithm is biased toward awake techniques, traditional preoxygenation is preferable to fast track (4 breaths), and extra precautions should be taken prior to induction of anesthesia. These include recruitment of additional experienced personnel during the induction of anesthesia, immediate availability of the full complement of noninvasive and invasive airway management devices, including an unopened tracheostomy set.

Benumof J. Obstructive sleep apnea in the adult obese patient: implications for airway management. *Anes Clin N Am.* 20(2002):789–811.

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Kheterpal S, Martin L, Shanks A, et al. Prediction and outcomes of impossible mask ventilation: a review of 50,000 anesthetics. *Anesthesiology.* 2009;110(4):891–897.

Practice guidelines for management of the difficult airway. A report by the American Society of Anesthesiologists Task Force on Management of the Difficult Airway. *Anesthesiology.* 1993;78:597–602.

Practice guidelines for management of the difficult airway: an updated report by the American Society of Anesthesiologists Task Force on Management of the Difficult Airway. *Anesthesiology.* 2003;98:1269–1277.

C.3. How would you induce anesthesia? Describe the intubation technique.

This patient should be seen before arriving in the operative suite to ascertain nothing by mouth status, and a large bore intravenous access inserted. Nonsedative premedication, such as glycopryollate (0.4 mg), an anticholinergic used to dry the upper airway, and metoclopramide, a prokinetic, may be given in the operative suite to increase gastric emptying, because peak effects occur in approximately 45 minutes. The full complement of alternate airway, noninvasive and invasive (e.g., cricothyriodotomy set and surgical tracheotomy set) airway devices should be available.

On arrival in the operating room, the patient is placed on monitors, and given supplemental oxygen. Sedation is administered with very small doses of midazolam (4 mg), dexmedetomidine, a centrally acting α_2 agonist at the usual dosage range (1 μg per kg over 10 minutes, followed by 0.2 to 0.7 μg/kg/hour TBW), and incremental ketamine (10 mg per dose) as needed, titrated to have an awake, sedated cooperative patient. Dexmedetomidine appears to completely

override the sympathomimetic effects of the other medications. The decision is made to proceed with fiberoptic intubation via an oral route. Extensive oropharyngeal topicalization with 2% lidocaine, hypopharyngeal instillation with lidocaine using a mucosal atomization device, and airway blocks (glossopharyngeal, superior laryngeal, or translaryngeal) would provide excellent conditions. Five percent lidocaine ointment placed on the distal surface of an oral airway with a dollop of lidocaine ointment will come into contact with the mucosa adjacent to the superior laryngeal nerves, providing a suitable alternative to a peripheral block, if the external anatomy is unfavorable. The patient is ready for bronchoscopy when they will tolerate an intubating airway (Williams or Ovassapian) without coughing with a preloaded tracheal tube. Rarely, when anatomic features are unfavorable (e.g., poor mouth opening). fiberoptic intubation is performed via a nasal route. When the vocal cords are visualized, the vocal cords are sprayed with 4% lidocaine prior to entering the trachea. A tracheal tube is carefully passed, the position confirmed via auscultation and capnography. The patient is first anesthetized with high concentration sevoflurane, then switched to desflurane. After confirmation of acceptable chest wall mechanics, cisatracurium (0.2 mg per kg LBW) is given, and mechanical ventilation is initiated.

If the physical examination and past anesthetic record demonstrated easy orotracheal intubation, a rapid sequence intubation could be contemplated using either thiopental (3 to 5 mg per kg TBW) or propofol (2 mg/kg TBW) with succinylcholine (1 to 1.5 mg per kg TBW), with the patient positioned on a ramp.

If the intubating conditions are suboptimal, a noninvasive alternative airway management device is utilized. Both the C-Mac Videolaryngoscope (Karl Storz Endoscopy-America, Inc, Culver City), and the Airtraq Disposable Optical Laryngoscope (Prodol Systems, Spain) are excellent first-line, as well as back-up devices for the MO-OSA patient. They are described in greater detail in section C.5.

The key to success is extensive operator experience, thorough preparation, a helpful assistant, and willingness to return to a direct laryngoscopy when indicated.

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C.4. Why is it important to preoxygenate the obese patient? How would you do it? Compare the effectiveness of the four-maximum-breath and 3-minute techniques.

Thorough preoxygenation is important because intubation may take longer in morbidly obese than nonobese patients; moreover, because obese patients have a small intrapulmonary store of oxygen (low FRC), which is rapidly depleted (high oxygen consumption), they are at particularly high risk of hypoxemia.

Maximal total body preoxygenation, or denitrogenation, requires that the patient breathe 100% oxygen for at least 3 minutes in a well-sealed system, to fill the alveolar,

arterial, venous, and tissue spaces, and to obtain a pulse oximeter saturation (SpO_2) of 99% to 100%. This is superior to fast-track preoxygenation, or four-maximum vital capacity breaths. Farmery has created a model to describe the rate of oxyhemoglobin desaturation during apnea. Various preapnea arterial oxygen tensions produce a parallel family of apneic desaturation curves. Not all patients will deoxygenate at the same rate during apnea. In general, the morbidly obese adult desaturates the fastest. The child desaturates next fastest, followed by the moderately ill adult. Only the healthy adult, who desaturates the slowest, recovers from an intubating dose of succinylcholine just as hypoxia ensues.

Drummond et al. have shown that the rate of apneic desaturation after induction of anesthesia is related to the BMI. They suggest that three vital capacity VC breaths of 100% oxygen will allow for 3 minutes of apnea before the onset of hypoxemia. In their study, without preoxygenation, only 1 minute elapsed before significant desaturation occurred. Valentine et al. compared the effectiveness of the four-maximum-breath and 3-minute techniques in elderly patients. They found similar peak oxygen saturation values after preoxygenation with these two techniques. However, a significantly shorter time to all levels of desaturation was associated with the four-maximum-breath method when the patients were kept apneic and exposed to room air. The average times to 90% saturation were $3\frac{1}{2}$ minutes in the four-breath group and $6\frac{1}{2}$ minutes in the 3-minute group. Nakatsuka et al. recommend using pulse oximetry to achieve an Spo_2 of 99% to 100% during induction to ensure maximal oxygen availability and safe duration of apnea (159 ± 60 seconds) in morbidly obese patients. Benumof et al. recommend oxygen insufflation into the pharynx during laryngoscopy through a nasopharyngeal catheter.

Pre-induction CPAP has been advocated both to improve oxygenation, and to decrease atelectasis. Since apnea tolerance time is decreased in both morbidly obese and OSA patients, the triple airway maneuver (mandibular advancement, neck extension, and mouth opening) should be performed if mask ventilation is contemplated.

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C.5. There are many new airway devices on the marketplace. Which of these devices have been particularly successful on the morbidly obese or OSA patient?

In the 2003 iteration of the Difficult Airway Algorithm, the Laryngeal Mask Airway (LMA North America, San Diego, CA), the most commonly used supraglottic airway at

the time, was added. Inclusion of the LMA into the Algorithm emphasized that being able to ventilate through a temporary airway: 1) returns the patient to the elective branch of the algorithm, since they are being ventilated and oxygenated, 2) may often is all that was required for patient management, 3) provides a bridge for insertion of a definitive airway. As used in the Algorithm, the "LMA" should not be interpreted as endorsement of any particular manufacturer or product. Since implementation of the first Difficult Airway Algorithm, new and improved Laryngeal Mask Airway products have been developed. There has also been development of new airway devices, and new classes of product lines of other devices.

Many of the devices mentioned in the Algorithm either have fallen into disuse (e.g., retrograde intubation), have been supplanted by newer devices (e.g., tracheoesophageal combitube), or are not commonly utilized by the clinicians (e.g., rigid laryngoscopy). The Algorithm is in need of an update. In addition, there are no large scale studies comparing the performance of the newer devices on either the morbidly obese or OSA populations.

In the intervening period since 2003, there have been several advances in airway management. The first is the advent of affordable, high quality video laryngoscopes. The most promising of these for the severely obese or obstructive sleep apnea (MO/OSA) patient appears to be the C-Mac. The C-Mac is a videolaryngoscope based upon CMOS (complementory metal oxide semiconductor) technology, similar to a cell phone camera. The C-Mac is an unchannelled device, with high quality optical resolution, and may be used either for direct laryngoscopy, like a traditional laryngoscope, or indirect laryngoscopy. Digital photographs or videclips may be easily taken by the laryngoscopist with the C-Mac. Other unchannelled videolaryngoscopic devices, which have been used for this population include the GlideScope and the McGrath videoscope (Shippey). Although glottic visualization is frequently successful, intubation may be problematic, and right palatopharyngeal arch perforation has been reported secondary to blind insertion of the tracheal tube from the back of the pharynx to resurfacing within the camera's visual field at the laryngeal inlet. This complication is more likely to occur when lateral pharyngeal wall crowding occurs, as in MO with jowls, or severe OSA.

The second advance in airway management is the development of a new class of airway device: the channeled, disposable optical laryngoscope. The Airtraq (Prodol Systems, Spain) is the only device in this category. This device has been very successful in the MO/OSA patient. Advantages include portability, being able to intubate in a semi Fowler position "face-to-face", high retention success rate for the novice or infrequent practitioner, and being an excellent conduit for FOB. Intubating may be accomplished in a neutral neck position with little mouth opening.

The third advance in airway management is the development of better airway "bridges" and short-term ventilatory support devices. The LMA Fastrach, or intubating LMA (LMA North America, San Diego, CA), provides a method of oxygenating and ventilating while obtaining a definitive airway. The I-Gel (Intersurgical Complete Respiratory Systems, Berkshire, UK) provides cuffless, high quality perilaryngeal airway with a gastric decompression lumen. The LMA Supreme (LMA North America, San Diego, CA) is a supraglottic airway salvage device with a gastric decompression port that incorporates features of the LMA Unique, ProSeal and Fastrach.

Older propriety rigid laryngoscopes (e.g., Bullard Elite Laryngoscopes [Circon ACMI, Racine, WI], UpsherScope Ultra [Mercury Medical, Clearwater, FL] Wu Scope [Achi Corp, Fremont, CA] have been used effectively on morbidly obese patients. Of the rigid laryngoscopes, the Bonfils Retromolar Intubating Fiberscope [Karl Storz Endoscopy-America, Inc, Culver City]) has the best optical resolution, and is particularly helpful in cases with limited mouth opening. A tracheoesophageal Combitube (Tyco, Bermuda) is a useful airway salvage device in the morbidly obese patient.

The final advance in airway management is the development of high quality, single-use metal laryngoscope blades, which appear to have superior success rates compared with reusable metal laryngoscope blades in rapid sequence induction (RSI) of anesthesia (Amour). For the MO/OSA patient with a challenging airway, FOB remains the gold standard. FOB has substantial limitations, however, such as limited availability, a long learning curve, a low retention rate, equipment fragility, longer set up time, longer intubation time, and few absolute indications (mostly lower airway pathology). As the advanced airway management devices improve, and clinician experience grows, the need for FOB should continue to decline.

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C.6. How would you maintain general anesthesia? What agents would you choose?

Although the ideal maintenance anesthetic for morbidly obese patients undergoing laparoscopic surgical procedures is a matter of some discussion, there is support in the literature for a technique comprising insoluble anesthetic gases resistant to metabolic degradation and without lipid depot compartmentalization, combined with rapid return of airway reflexes, plus intravenous agents that are either hydrophilic, spontaneously degrade in vivo, or are ultrashort acting.

Of the potent inhalation agents, desflurane has several advantages; it is insolubile, has a faster wake-up, a faster return of airway reflexes, and a decreased amount of hepatometabolism. Obesity increases the biotransformation of the inhalation

anesthetics, resulting in increased serum toxic products of metabolism. Because of the frequent presence of coexisting liver dysfunction in the morbidly obese (75% have hepatic steatosis, and 25% have severe hepatic dysfunction), and the absence of a clear correlation between liver function tests and hepatic dysfunction, it would seem logical to use the agent with the lowest percentage of hepatometabolism, desflurane (0.02%), compared with isoflurane (0.2%), and sevoflurane (4% to 5%). An agent with a low blood–gas solubility coefficient is better because there will be a smaller body reservoir available for metabolism, and a faster time to steady state at the target organ, the brain. Of the inhaled agents, desflurane has the fastest wake-up, which is followed by sevoflurane, then by isoflurane. Desflurane also has the fastest return of airway reflexes, followed by sevoflurane.

Although nitrous oxide, a weak inhalation anesthetic, has certain advantages, such as a low blood–gas solubility coefficient (0.46), it is not recommended for maintenance use, because it causes intestinal inflation and is emetogenic. Nitrous oxide use is contraindicated with preexisting severe pulmonary hypertension, a condition more common in the severely obese. Short duration use of nitrous oxide, particularly during the surgical closure facilitates offset of relatively lipid soluble agents.

Remifentanil is the intraoperative narcotic of choice because of its rapid onset, consistent profile, and rapid offset. Although it is lipophilic, it has a half-life of 5 minutes, and therefore never enters the lipid compartment. Remifentanil has an equal volume of distribution (VD) calculated as LBW, relative to normal-weight individuals. It is dosed by infusion, starting at 0.2 μg/kg/minute LBW. The lipophilic opioids, fentanyl and sufentanil, that are dosed by TBW, and may cause delayed respiratory depression in the high-risk patient, especially OSAHS, are less than ideal.

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C.7. Which muscle relaxants would you use?

Severe obesity, per se, does not increase the risk of "full stomach." Although peak gastric volume is increased, the rate of gastric emptying is identical to that of the non-obese. Hence fasted obese patients should not be at increased risk of aspiration. Co-morbidities such as gastroesophageal reflux, hiatal hernia, peptic ulcer disease, esophageal pathology, and gastroparesis, however, may increase risk of aspiration.

The risk of aspiration must be weighed against the risk of loss of airway. MO/OSA increases the risk of DMV. Modified RSI has the advantage over RSI of allowing confirmation of ability to mask ventilate, prior to administration of muscle relaxant. Once a muscle relaxant is administered to a severely obese patient, there should be the expectation that should mask ventilation be difficult, the airway must be secured, and adequate spontaneous recovery may not occur prior to the onset of severe hypoxemia. This includes succinylcholine, with a wake up time of approximately 10 minutes, following an intubating dose. Smaller than ideal doses may lead to suboptimal intubating conditions, with attendant risks, such as laryngospasm. If a patient who has received a muscle relaxant cannot be intubated, and can only be marginally ventilated, succinylcholine is a better choice than rocuronium, since adequate spontaneous recovery is much faster.

Succinylcholine and rocuronium are the choices for RSI and modified RSI. Succinylcholine is dosed by TBW, because the plasma cholinesterase activity increases in proportion to the BMI. Rocuronium is dosed according to the LBW. Once the neuromuscular reversal agent sugammadex becomes available, a fast-acting nondepolarizing agent such as rocuronium will become a safe alternative to succinylcholine. Rocuronium has a poor dose response curve, and, like vecuronium, undergoes enterohepatic recirculation, and is metaqbolized by the liver. In a patient population with a high incidence of hepatic steatosis, rocuronium is not an ideal choice.

When an awake technique is chosen for securing the airway, a nondepolarizing muscle relaxant may be administered once tracheal intubation has been confirmed. For maintenance of anesthesia, cisatracurium is the preferred muscle relaxant. It is dosed by IBW plus 20% to 25%, or LBW. It has a predictable dose–response curve, and no prolongation of recovery due to organ-independent recovery or Hoffman elimination.

Dense muscle relaxation is required for laparoscopic bariatric surgical procedures, to facilate ventilation, to maintain adequate space for visualization and manipulation of the surgical instruments, and to permit the introduction of surgical instruments and the removal of excised tissues. Intraoperative contracture of the abdominal musculature, due to inadequate muscle relaxants, may increase intra-abdominal pressure during pneumoperitoneum, driving carbon dioxide out from the inflated abdominal cavity through the trocar sites. The adequacy of intraoperative neuromuscular blockade may therefore be assessed by the anesthesiologist, by following both the train-of-four and the inflation pressures necessary for excellent surgical conditions.

A peripheral nerve stimulator should be used to monitor the extent of relaxation and to avoid underdosing or overdosing of nondepolarizing neuromuscular blocking agents. Extubation should only occur after documentation of full baseline train-of-four ($T_4/T_1 > 0.9$), and return of extubation criteria. Reversal agents should be given in appropriate doses.

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C.8. Can regional anesthesia be used intraoperatively and postoperatively to decrease opioid requirements? What are the advantages and disadvantages of regional anesthesia? What are some of the newer techniques available?

Several regional anesthetic techniques may be used intraoperatively and postoperatively to decrease opioid requirements. Thoracic epidural anesthesia and analgesia (TEAA), the best studied of these, has been combined with light general anesthesia, and found by some authors to have a good side effect profile, and to offer advantages over general anesthesia, such as decreased postoperative drowsiness, nausea, and respiratory depression, improved cardiovascular function (decreased left ventricular stroke work index), decreased oxygen consumption, earlier return of lung function, less pulmonary complications, earlier return of gastrointestinal function, and shorter hospitalization times than PCA. Regional anesthesia/analgesia remains underutilized (PCA is >90%) in this patient population, because of the following disadvantages: technical difficulties, logistics (slows operating room case flow), increased incidence of epidural failure and catheter dislodgment, decreased epidural space from intra-abdominal pressure causing unpredictable spread of local anesthetics, variable block level, and increased incidence of wound infection, possibly from microdehiscence. Both patient-controlled epidural analgesia (PCEA) and PCA offer excellent pain reduction scores without respiratory depression when properly used. It is recommended that epidurals be inserted in the sitting position, using ultrasonic guidance. Laparoscopic cases currently comprise approximately 75% of bariatric surgical volume, reducing the need for postoperative analgesic services.

Other regional anesthesia techniques in the morbidly obese, that have been less studied include continuous spinal anesthesia and analgesia (CSAA), and intrathecal opioids (ITO). CSAA may be used with or without general anesthesia. The advantages are the same as for TEAA, except that technique is technically easier, there is a denser block, motor component, and more predictable and controllable dermatomal spread. With all of these techniques, local anesthetic dose is typically 75% to 80% of the dose for the nonobese patient. Local anesthetics and opioids act synergistically at decreased dosages. Respiratory depression is more common using hydrophilic agents (e.g., morphine) than lipophilic agents (e.g., fentanyl). Respiratory depression induced by morphine follows a longer time course (1 to 18 hours) than with fentanyl (minutes to 2 hours). It is important to identify those individuals with risk factors for neuraxial respiratory depression risk factors: excessive or repeated doses, concomittent sedatives or hypnotics, advanced age, demonstrated lack of opioid tolerance, increased intra-abdominal pressure (e.g., pneumoperitoneum), and severe OSAHS patients, who may be at risk for massive pharyngeal collapse. Our patient was not a candidate for regional anesthesia/analgesia for this reason.

Some of the newer techniques available include multimodal perioperative analgesia, nonopioid analgesia, and dexmedetomidine. Multimodal perioperative analgesia, a combination of preincisional local anesthetics, nonsteroidal antiinflammatory drugs and PCA, uses preemptive analgesia. Nonopioid analgesia uses a combination of methylprednisolone, ketorolac, clonidine, lidocaine, ketamine infusion, and magnesium sulfate infusion to decrease side effect profile, and speed recovery. Dexmedetomidine, a centrally acting α_2 agonist, may be used intraoperatively and postoperatively to decrease opioid requirements.

For peripheral surgical procedures, the use of peripheral nerve blocks is advocated in the morbidly obese, provided that adequate landmarks exist.

Relatively few studies exist on the use of regional anesthesia to facilitate postoperative pain management following bariatric surgery. The current emphasis is on fast tracking these patients, by using ultra-short acting agents and agents that minimize postoperative respiratory depression, such as remifentanil and dexmetomidine. Early extubation and ambulation are preferable for all but the highest risk candidates.

Charghi R, Backman S, Christou N, et al. Patient controlled iv analgesia is an acceptable pain management strategy in morbidly obese patients undergoing gastric bypass surgery. A retrospective comparison with epidural analgesia. *Canadian J Anesth*. 2003;50:672–678.

Choi YK, Brolin RE, Wagner BK, et al. Efficacy and safety of patient-controlled analgesia for morbidly obese patients following gastric bypass surgery. *Obes Surg*. 2000;10: 154–159.

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Otsu I, Thirlby RC, Allen HW. Patient controlled thoracic epidural analgesia after gastric bypass surgery for morbid obesity. *Reg Anesth Pain Med*. 2001;26:A117.

Schumann R, Shikora S, Weiss J, et al. A comparison of multimodal perioperative analgesia to epidural pain management after gastric bypass surgery. *Anesth Analg*. 2003;96:469–474.

C.9. What is the effect of narcotics on the sphincter of Oddi? Is pharmacologic treatment indicated?

Subcutaneously administered morphine, 10 mg, increases the pressure in the common bile duct more than 10-fold within 15 minutes; this effect can be present for 2 hours or longer. Opioids can cause sphincter of Oddi spasm, which can interfere with intraoperative cholangiography. At equianalgesic doses, fentanyl, and morphine cause larger increases in biliary pressure than meperidine or pentazocine. Butorphanol and nalbuphine probably do not cause sphincter of Oddi spasm. Morphine is not a good analgesic choice for biliary tract surgery. Atropine partially prevents opioid-induced biliary spasm. Glucagon, nalbuphine, nitroglycerine, volatile anesthetics, and opioid antagonists, such as naloxone, effectively prevent or prophylax opioid-induced biliary spasm. Glucagon, 1 or 2 mg intravenously, is the drug of choice, and is also used to decrease upper gastrointestinal tract motility (e.g., for endoscopic procedures). The only common side effects are slight increase in heart rate, and transient hyperglycemia.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2009:474–475.

Radnay PA, Duncalf D, Novakovakovic M, et al. Common bile duct pressure changes after fentanyl, morphine, meperidine, butorphanol, and naloxone. *Anesth Analg*. 1984;63:441.

C.10. During surgery, arterial blood gases showed pH 7.35; Pao_2, 57 mm Hg; $Paco_2$, 52 mm Hg; FIo_2, 0.6; mechanical ventilator V_T, 1.0 L; and ventilatory rate, 15 breaths per minute. The following changes were made to the ventilatory parameters: 10 cm H_2O positive end-expiratory pressure (PEEP) was added, and the V_T was increased to 1.2 L. Twenty minutes later, an arterial blood gas showed pH 7.32; Pao_2, 55 mm Hg; and $Paco_2$, 55 mm Hg. What is the explanation for these changes?

Both blood gases are significant for respiratory acidosis and hypoxemia. It is important to look at the surgical field, examine the patient, auscultate the chest, and check the position of the tracheal tube to rule out endobronchial intubation, kinking of the

tube, or mucous plugging. While performing a differential diagnosis, it is advisable to increase the FIO_2, ascertain that the level of pneumoperitoneum is less than 20 cm Hg, note the peak airway pressure, hand bag the patient, and consider a bronchial dilator. FOB inspection of the airway through the tracheal tube may be helpful in certain cases. If the patient remains hypoxic despite these efforts, it may be necessary to inform the surgeon, halt the surgical procedure, and remove the pneumoperitoneum while searching for an etiology.

In the absence of life-threatening events, there are several pathophysiologic explanations for these blood gases. Endotracheal tube movement is more common in severely obese patients. Usually, PEEP increases Pao_2, and increased V_T decreases the $Paco_2$. Occasionally, PEEP and increased V_T may paradoxically decrease Pao_2, and increase the $Paco_2$, especially in morbidly obese patients. There are several reasons for this. First, high airway pressure can interrupt pulmonary capillary blood flow at the uppermost portions of the lung at peak inspiration. Since these areas already have high ventilation/perfusion, further decreases in perfusion result in an increase in physiologic dead space (V_D/V_T) and increased $Paco_2$. The impeded blood flow will be redistributed to areas of lung that are not affected by the high airway pressure, resulting in an increase in intrapulmonary shunt (Q_S/Q_T) and a decrease in PaO_2. Second, high airway pressures decrease venous return and CO, which may decrease Pao_2 and increase $Paco_2$. Third, high V_T and high airway pressures may create low lung water pulmonary edema from volutrauma and barotrauma. Fourth, overdistension of the pleura and turbulent airflow may result from excessive ventilator settings. This may precipitate bronchospasm in susceptible patients, such as asthmatics, especially when associated with light anesthesia. Fifth, at excessive airway pressures, there may be rupture of a preexisting bleb or bulla, possibly necessitating chest tube insertion.

Eichenberger A, Prioetti S, Wicky S, et al. Morbid obesity and postoperative pulmonary atelectasis: an underestimated problem. *Anesth Analg.* 2002;95:1788–1792.

Ezri T, Hazin V, Warters D, et al. The endotracheal tube moves more often in obese patients undergoing laparoscopy compared with open abdominal surgery. *Anesth Analg.* 2003;96(1):278–282.

Hines RL, Marschall KE. *Stoelting's Anesthesia and Co-existing Disease.* 5th ed. Philadelphia: Churchill Livingstone, Elsevier; 2008:297–306.

Nguyen NT, Anderson JT, Budd M, et al. Effects of pneumoperitoneum on intraoperative pulmonary mechanics and gas exchange during laparoscopic gastric bypass. *Surg Endosc.* 2004;18:64–71.

Sprung J, Whalley DG, Falcone T, et al. The effects of tidal volume and respiratory rate on oxygenation and respiratory mechanics during laparoscopy in morbidly obese patients. *Anesth Analg.* 2003;97:268–274.

Whalen FX, Gajic O, Thompson GB, et al. The effects of the alveolar recruitment maneuver and positive end-expiratory pressure on arterial oxygenation during laparoscopic bariatric surgery. *Anesth Analg.* 2006;102:298–305.

C.11. What is apneic oxygenation? Who did the pioneer study?

Draper and Whitehead conducted the pioneer study on apneic oxygenation in 1944. Apneic oxygenation (formerly known as diffusion respiration) is actually caused by mass movement oxygenation. When the lungs are completely denitrogenized with oxygen and the airway is connected to an oxygen source, continuous oxygenation takes place by mass movement. Normally, every minute, 230 mL of oxygen is removed from the alveoli for metabolism and 200 mL of CO_2 is produced and eliminated from the lungs. When a person is apneic, only 10% of CO_2 accumulates in the alveoli,

and 90% of CO_2 stays in the blood as bicarbonate. Consequently, 250 mL of oxygen is removed from the lungs and 20 mL of CO_2 accumulates in the lungs, creating a 230-mL vacuum effect and sucking in oxygen. Carbon dioxide tension continues to rise because no elimination occurs during apnea. The total pressure in the alveoli is constant, so the decrease in PO_2 equals the rise in Pco_2, ranging from 3 to 6 mm Hg per minute. If the patient had been breathing 100% oxygen before respiratory arrest, the starting alveolar PO_2 would be about 650 mm Hg, and therefore, the patient could theoretically maintain Pao_2 above 100 mm Hg for about 100 minutes of apnea provided that the airway remained clear and connected to 100% oxygen. However, patients will die of severe respiratory acidosis (pH <6.80) before hypoxemia occurs. Moreover, as seen in suffocation, gross hypoxia supervenes after about 90 seconds if apnea with airway occlusion follows air breathing at the FRC. When the airway is patent and the ambient gas is air, gross hypoxia supervenes after about 2 minutes of apnea, as seen during intubation without preoxygenation. However, if the patient is preoxygenated for 3 minutes, gross hypoxia will not occur until 6 minutes of apnea for normal-weight patients and until about 3 minutes of apnea for morbidly obese patients. Apneic oxygenation is an older technique that is not recommended for morbidly obese patients. Aside from hypoxia and hypecarbia, it may lead to atelectasis, or derecruitment of West Zone 3.

A much more useful maneuver in severely obese patients is to utilize one hundred per cent oxygen and PEEP, during both induction and emergence from general anesthesia.

Coussa, Proietti S, Schnyder P, et al. Prevention of atelectasis formation during induction of general anesthesia in morbidly obese patients. *Anesth Analg*. 2004;98:1491–1495.

Edmark L, Kostova-Aherdan K, Enlund M, et al. Optimal oxygen concentration during induction of general anesthesia. *Anesthesiology*. 2003;98:28–33.

Gander S, Frascarolo P, Suter M, et al. Positive end-expiratory pressure during induction of general anesthesia increases duration of nonhypoxic apnea in morbidly obese patients. *Anesth Analg*. 2005;100:580–584.

Jense HG, Dubin SA, Silverstein PL, et al. Effect of obesity on safe duration of apnea in unanesthetized humans. *Anesth Analg*. 1991;2:89–93.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 6th ed. Philadelphia: Elsevier Butterworth-Heinemann; 2005;160–161.

C.12. What is diffusion hypoxia? How do you prevent it?

Fink and colleagues in 1954 first reported diffusion hypoxia during recovery from nitrous oxide-oxygen anesthesia. A mild degree of hypoxia can develop for more than 10 minutes when nitrous oxide-oxygen anesthesia is concluded and the patient is allowed to breathe room air. The arterial oxygen saturation can fall 5% to 10% and often reaches values less than 90% (Pao_2 <60 mm Hg). This occurs at the times when nitrous oxide is eliminated rapidly through the lungs. Nitrous oxide is 35 times more soluble in blood than nitrogen. Therefore, the amount of nitrous oxide diffused from blood to alveoli is much more than the amount of nitrogen diffused from alveoli to blood. Hence, alveolar oxygen is diluted by nitrous oxide. Diffusion hypoxia can be prevented by the inhalation of high concentrations of oxygen for several minutes before the patient is allowed to breathe room air.

Diffusion hypoxia should not be allowed to occur in obese patients. There is no room for deep extubations in the MO/OSA patient. Patients should be fully awake, with baseline respiratory function. All anesthetics and analgesics, with the possible exception of dexmedetomidine, should be stopped. Many of the newer anesthesia

ventilators allow the use of pressure support ventilation during the emergence phase, which minimizes atelectasis. One hundred percent oxygen prior to, and during, extubation followed by a tight fitting face mask with pressure support, aids the patient in re-establishing ventilatory function, and assists in removal of trace anesthetic gas, until the patient is fully recovered.

Alvarez A, Brodsky JB, Lemmens H, et al., eds. *Morbid Obesity: Peri-operative Management*. 2nd ed. Cambridge: Cambridge University Press; 2010:124–137.

El-Solh AA, Aquilina A, Pineda L, et al. Noninvasive ventilation for prevention of post-extubation failure in obese patients. *Eur Respir J*. 2006;28:588–595.

Fink BR. Diffusion anoxia. *Anesthesiology*. 1955;16:511–519.

Fink BR, Carpenter SL, Holaday DA, et al. Diffusion anoxia during recovery from nitrous oxide-oxygen anesthesia. *Fed Proc*. 1954;13:354.

Sheffer L, Steffenson JL, Birch AA. Nitrous oxide-induced diffusion hypoxia in patients breathing spontaneously. *Anesthesiology*. 1972;37:436.

D. Postoperative Management

D.1. When will you extubate this patient? What are the extubation criteria?

In the past, prophylactic ventilatory support throughout the first postoperative night was occasionally utilized for the morbidly obese OSAHS or OHS patient having an open abdominal weight reduction procedure. Currently, this is rarely the case; due to the huge yearly increases in the number of bariatric surgeries in the United States (16,000 in the early 1990s, to 200,000 in 2010), advanced laparoscopic experience of the surgeons, and advances in the anesthetic care of the morbidly obese, most patients are extubated in the operating room at the conclusion of surgery as soon as the following extubation criteria are met:

- Intact neurologic status, fully awake and alert, with head lift greater than 5 seconds
- Hemodynamic stability
- Normothermia. The core temperature is above 36° C.
- Train-of-four (TOF) reversal documented by peripheral nerve stimulator (T_4/T_1 >0.9). Full reversal of neuromuscular blocking agents.
- Respiratory rate (>10 and <30 breaths per minute)
- Baseline peripheral oxygenation, as judged by pulse oximeter (SpO_2 >95% on FIO_2 of 0.4).
- Rarely, if an arterial line is present, an arterial blood gas may be checked. Acceptable blood–gas results (FIO_2 of 0.4; pH, 7.35 to 7.45; PaO_2, >80 mm Hg; $PaCO_2$, <50 mm Hg).
- Acceptable respiratory mechanics: negative inspiratory force (NIF) (>25 to 30 cm H_2O; vital capacity (VC) >10 mL/kg IBW; V_T >5 mL/kg IBW).
- Acceptable pain control
- No demonstrated or suspected laboratory abnormalities

Extubation criteria should be used systematically in obese patients. In all cases, an attending anesthesiologist with advanced airway skills must be in attendance for extubation. Emergency tracheal reintubation may be necessary. Patients with documented difficult airway should be extubated per protocol. Patients with OSAHS, OHS, and the PS have higher incidence of postoperative respiratory dysfunction. They require special attention before and after extubation, and occasionally warrant a monitored bed for observation.

Alvarez A, Brodsky JB, Lemmens H, et al., eds. *Morbid Obesity: Perioperative Management*. 2nd ed. Cambridge, Cambridge University Press 2010;2:124–137.

Perilli V, Sollazzi, Bozza P, et al. The effects of the reverse Trendelenburg position on respiratory mechanics and blood gases in morbidly obese patients during bariatric surgery. *Anesth Analg*. 2000;91:1520–1525.

Wong AB, Moore MSR. Positioning ob obese patients in out-of-operating room locations. *Anesth Analg*. 2007;104:1306.

D.2. What are the major early postoperative complications in the morbidly obese patient? How do health-related risks correlate with obesity? What factors correlated statistically with perioperative mortality?

The major early postoperative complications in the morbidly obese are mostly related to the pulmonary and cardiovascular systems. Postanesthetic hypoxemia, respiratory depression, early ventilatory failure with need for reintubation, positional ventilatory collapse, hemodynamic instability, postoperative nausea and vomiting, and venous thromboembolism are some common examples. Early surgical complications include anastomotic closure with bowel obstruction, anastomotic leak, surgical bleeding, internal hernias with incarcerated bowel and wound infection.

At any given weight, the perioperative risk is greater for central obesity than for peripheral obesity, and for patients with preexisting severe comorbidity, especially OSAHS.

The major perioperative risk of death correlates statistically with BMI, preexisting hypertension, pulmonary embolus, and anastomotic leak.

Ahmad S, Nagle A, McCarthy RJ, Fitzgeral PC, et al. Postoperative hypoxemia in morbidly obese patients with and without obstructive sleep apnea undergoing laparoscopic surgery. *Anesth Analg*. 2008;107;138–143.

Fernandez A, Adolfo Z, Demaria E, et al. Multivariate analysis of risk factors for death following gastric bypass for treatment of morbid obesity. *Ann Surg*. 2004;239(5):698–703.

Orhan-Sungar M, Kranke P, Sessler D, Apfel CC. Does supplemental oxygen reduce postoperative nausea and vomiting? A meta-analysis of randomized trials. *Anesth Analg*. 2008;106:1733–1738.

Weingarten TN, Flores AS,1 McKenzie JA, Nguyen LT. Obstructive sleep apnoea and perioperative complications in bariatric patients. *Br J Anaesth*. 2011;106(1):131–139.

D.3. How does position affect respiratory function in the obese patient?

In the supine position, intra-abdominal contents shift the diaphragm rostrally resulting in diaphragmatic dysfunction, decreased FRC, airway closure, increase in venous admixture (Q_S/Q_T), decreased Pao_2, and possibly positional ventilatory collapse. The FRC increases 30% in obese patients by changing from the supine position to the sitting position, both in nonsurgical and postlaparotomy patients. Recovery should take place in a semi-Fowler position (head up at an angle of 30 to 45 degrees) as soon as these patients are hemodynamically stable. Other benefits of a semisitting position are decreased superior vena cava pressure, decreased incidence of positional injuries, which are more common in the morbidly obese. Patients recovered in the semi-Fowler position, who are in need of eventual emergent mask ventilation or tracheal reintubation, present better conditions for the laryngoscopist. There is a higher incidence of tracheal tube misplacement in the morbidly obese; care should be taken when positioning these patients in a semi-Fowler position.

Brodsky JB, Lemmons HJ, Brock-Utne, et al. Anesthetic considerations for bariatric surgery: proper positioning is important for laryngoscopy. *Anesth Analg.* 2003;96:1841–1842.

Ezri T, Hazin V, Warters D, et al. The endotracheal tube moves more often in obese patients undergoing laparoscopy compared with open abdominal surgery. *Anesth Analg.* 2003;96(1):278–282.

Memtsoudis S, Spencer Liu S, Ma Y, et al. Perioperative pulmonary outcomes in patients with sleep apnea after noncardiac surgery. *Anesth Analg Jan.* 2011;112(1):113–121.

D.4. How would you prevent postoperative atelectasis?

In the past, bariatric surgical procedures were often performed open, with an incidence of postoperative atelectasis of 45%. Approximately 75% are now performed laparoscopically, so the incidence would be expected to decline substantially.

Early ambulation, chest physical ambulation with incentive spirometry, and effective coughing are encouraged to improve respiratory function. Prolonged recumbency is avoided whenever because of its adverse effects on the ventilation/perfusion ratio. Careful titration of postoperative analgesics is emphasized to prevent splinting from pain and hypoventilation from excessive sedation.

Babatunde O, Jones S, Jones D, et al. Anesthetic considerations for bariatric surgery. *Anesth Analg.* 2002;95:1793–1805.

Chung SA, Yuan H, Chung F. A systematic review of obstructive sleep apnea and its implications for anesthesiologists. *Anesthesiologists.* 2008;107:1543–1563.

Schumann R, Jones SB, Cooper R, et al. Update on best practice recommendations for anesthetic perioperative care and pain management in weight loss surgery 2004–2007. *Obesity (Silver Spring).* 2009;17:889–894.

D.5. How long would you prescribe supplementary oxygen postoperatively?

The incidence of postanesthetic hypoxemia (Pao_2 <60 mm Hg) is increased from a baseline of 25% to 30% in the nonobese to 75% in the obese. For a routine case on an otherwise healthy patient with simple obesity, supplemental oxygen in the PACU is probably sufficient. In most morbidly obese patients with comorbidities, oxygen should be prescribed for 24 to 72 hours. The morbidly obese patient with severe OSAHS on CPAP or BIPAP will usually have continuation of their therapy overnight, be recovered in a semi-Fowler position (at an angle of 30 to 45 degrees) and should have individualized care, with continuous pulse oximetry, and respiratory monitoring. At The New York-Presbyterian Hospital, most of these patients are discharged to home on the third or fourth postsurgical day.

Bell RL, Rosenbaum SH. Postoperative considerations for patients with obesity and obstructive sleep apnea. *Anesthesiol Clin N Am.* 2005;23:493–500.

Downs JB. Prevention of hypoxemia: the simple, logical, but incorrect solution. *J Clin Anesth.* 1994;6:180.

Gross JB, Bachenberg KL, Benumof JL, et al. Practice guidelines for the perioperative management of patients with obstructive sleep apnea. *Anesthesioogy.* 2006;104: 1081–1093.

Schumann R, Jones SB, Cooper R, et al. Update on best practice recommendations for anesthetic perioperative care and pain management in weight loss surgery 2004–2007. *Obesity (Silver Spring).* 2009;17:889–894.

D.6. How would you control postoperative pain?

In more than 90% of bariatric surgical procedures, analgesia is provided postoperatively by parenteral narcotics using patient-controlled analgesia (PCA), as it was for our patient. PCA has been shown to be safe and effective in the morbidly obese patient population. It has many advantages: PCA is simple to use, saves nursing time, involves minimal time delay between patient perception of pain and therapy. There is less splinting and PFTs return early. PCA also facilitates early ambulation and shortens hospital stay. Dosing of morphine, the gold standard, needs to be individualized. Hydromorphone is also frequently used. Dose regimens need to be individualized, according to pain control and side effect profile. There have been some cases of respiratory complications in the MO-OSAHS patient, so extra viligence is needed in this group. PCA dosages for the morbidly obese in the opioid naïve, based on IBW, are as follows:

- Morphine sulfate 20 μg/kg IBW
- Hydromorphone 4 to 5 μg/kg IBW
- Fentanyl 1 μg/kg IBW
- Methadone 20 μg/kg IBW

All settings are every 10 minutes, without continuous rate, at 80% of the calculated maximum doses. Although the opioids have different lipid solubilities, PCA doses were originally formulated using IBW, and this practice has not changed. As we are titrating to individual patient satisfaction, there is room for post-treatment dose modification.

Intravenous infusions of opioids may also be administered in a monitored setting. In the past, opioids have been administered intramuscularly. Although this route has been shown to be effective, intramuscular injection is not advisable in the morbidly obese, because of unpredictable pharmacodynamics, arising from inadvertent injection into lipid tissue.

There are three regional anesthetic/analgesic options: TEAA/PCEA, ITO, and continuous spinal anesthesia/patient-controlled intrathecal analgesia (CSA/PCIA). All of these may be used intraoperatively with or without light general anesthesia (GA). They offer similar side effect profiles and will be described together. *PCEA*, the most commonly used of these, has numerous theoretical advantages. At a lower dose compared with parenteral opioids, there are few side effects and serious complications, effective analgesia, faster recovery, less respiratory complications, decreased total body oxygen consumption, improved cardiac function (decreased left ventricular stroke work index [LVSWI]), and shorter hospitalization times compared with PCA. PCEA dosages in the morbidly obese should be decreased 75% to 80%, due to decreased volume of the epidural space from increased intra-abdominal pressure. PCEA is strongly recommended when feasible, yet remains underutilized. Patients should be positioned in a sitting position for epidural catheter insertion, and ultrasonography guidance is recommended. Disadvantages include a higher rate of wound infection, possibly because of microdehiscence from faster return of gastrointestinal function, and the risk of neural injury. There is frequent technical difficulty with catheter insertion, which slows operating room case flow. There is a higher rate of inadequate function, catheter migration and replacement, and variable block height. Side effects include excessive drowsiness, postoperative nausea and vomiting, pruritis, and urinary retention. Respiratory depression occurs rarely, and is more common with hydrophilic (e.g., preservative-free morphine sulfate [PFMS]) than with hydrophilic agents. With PFMS it may occur from 1 hour until 18 hours. With fentanyl or sufentanil it may occur from minutes until 2 hours. Neuraxial opioid respiratory depression risk factors include advanced age, excessive or repeated doses, lack of opioid tolerance, use of concomitant sedatives or hypnotics, increased intra-abdominal pressure (e.g., pneumoperitoneum), and severe OSAHS, which may precipitate massive pha-

ryngeal collapse. *CSA/PCIA* with light GA has been used for gastroplastic surgery. It is technically easier to perform than TEAA/PCEA, and produces a denser block with motor component, which is more predictable and controllable. *IT* opioids, with or without local anesthetics, are technically easier to administer, and offer an excellent alternative for appropriate surgical procedures. Other methods of controlling postoperative pain in bariatric surgery include preemptive analgesia through local anesthetic wound infiltration before and after surgery, pre- and intraoperative nonopioid drug combination (ketorolac, clonidine, lidocaine, ketamine, magnesium sulfate, and methylprednisolone), and perioperative dexmedetomidine.

Charghi R, Backman S, Christou N, et al. Patient controlled iv analgesia is an acceptable pain management strategy in morbidly obese patients undergoing gastric bypass surgery. A retrospective comparison with epidural analgesia. *Can J Anesth.* 2003;50:672–678.

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Rawal N, Sjostrand U, Christoffersson E, et al. Comparison of intramuscular and epidural morphine for postoperative analgesia in the grossly obese: influence on postoperative ambulation and pulmonary function. *Anesth Analg.* 1984;63:583–592.

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